Statistical Analysis Plan (SAP)

Trial: The effects of adding a diet intervention to exercise on hip osteoarthritis pain: the ECHO trial

Contents

Section 1. Administrative Information

1. Title

Effects of adding a diet intervention to exercise on hip osteoarthritis pain: the ECHO randomized controlled trial

2. Trial registration

Prospectively registered (ClinicalTrials.gov. Identifier: NCT04825483, 31/03/2023)

3. SAP version

Version: 1.0 Date: 6/14/2024

4. Protocol Version

This document has been written based on information contained in the ECHO study protocol version 3 dated 23/05/2023.

5. SAP Revisions

Not applicable.

6. Names and affiliations

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Signatures:

Signature of statistician responsible (Fiona McManus): Date: 11/6/2024

Signature of chief investigator (Prof Kim Bennell): Date: 14/6/2024

Section 2: Introduction

7. Background and rationale

Hip OA is a major public health problem and symptomatic hip OA affects one in four adults over their lifetime[1]. There is no cure for OA and joint replacement is reserved for end-stage disease. Clinical guidelines[2-6] recommend exercise as the core treatment for hip OA symptoms. However, recommendations for weight loss to manage hip OA symptoms are inconsistent, due to the absence of clinical trials in hip OA evaluating weight loss. Therefore, it remains uncertain whether weight loss in addition to exercise and regular physical activity is more beneficial for hip OA pain compared to exercise alone.

Clinical guidelines[2-6] including the 2019 American College of Rheumatology guidelines[5], recommend weight loss for hip OA based on evidence from clinical trials in knee OA. However, the 2019 Osteoarthritis Research Society International guidelines for hip OA management do not recommend weight loss for hip OA[2] due to the absence of clinical trials in hip OA evaluating weight loss. A reduction in body weight by at least 5% is recommended for improvement in clinical and mechanistic outcomes, however this is based on evidence in people with knee OA[5]. Irrefutable health benefits are associated with weight loss for those with overweight or obesity[7]. However, our systematic review and meta-analysis of clinical trials found that a combination of diet and exercise reduced knee OA pain compared to control, but not for diet only interventions compared to control[7]. Notably, the control was considered either an active (non-diet treatment) or no treatment (including placebo or waiting list)[7]. Evidence on the effectiveness of weight loss is urgently needed to inform treatment.

Among the myriad of weight loss strategies, a ketogenic very low calorie diet (VLCD) leads to greater short-term weight loss compared to low-fat diets[8] and low calorie diets[9]. This program is typically characterized by an intensive weight loss phase followed by a transition and maintenance phase. A systematic review and meta-analysis of ketogenic VLCDs found an average 14% reduction in body weight loss in studies with a ketogenic phase up to 12 weeks, with loss in body weight stable up to 2 years follow-up[9]. Additionally, a VLCD was associated with improvements in factors related to cardiovascular disease such as blood pressure, total cholesterol and triglycerides. Importantly, in combination with exercise, using nutritionally complete meal replacement products is considered safe in adults aged up to 80 years or older[10]. A VLCD is perceived as acceptable to people with knee OA[11], and our pilot study in hip OA (n = 18) demonstrated feasibility of a ketogenic VLCD and exercise intervention delivered remotely[12]. We observed an average of 10% [95% CI 8 to 12%] reduction in body weight at 3 months and no serious adverse events related to the diet program were reported[12].

8. Objectives

Study objectives:

Primary objective: To evaluate if a 6 month diet and exercise program results in significantly greater improvements in hip pain compared to an exercise only program at 6 months.

Secondary objectives:
To evaluate if a 6 month diet and exercise program results in significantly greater improvement in hip pain compared to an exercise only program at 12 months.

To evaluate if a 6 month diet and exercise program will improve other clinical outcomes (body weight,

body mass index, visceral fat mass, total body fat mass, other measures of hip pain, physical function, quality of life, perceived change in physical activity and hip problem) compared to an exercise only program at 6 months and 12 months.

Health economic objective:
To evaluate if a 6 month diet and exercise program is cost-effective at 12 months compared to an exercise only program.

Research hypotheses:

Primary alternative hypothesis: A 6 month diet and exercise program will improve self-reported pain in people with hip OA when compared to an exercise only program at 6 months.

Secondary alternative hypotheses:
A 6 month diet and exercise program will improve self-reported pain in people with hip OA when compared to an exercise only program at 12 months.

A 6 month diet and exercise program will improve other clinical outcomes (body weight, body mass index, visceral fat mass, total body fat mass, other measures of hip pain, physical function, quality of life, perceived change in physical activity and hip problem) compared to an exercise only program at 6 months and 12 months.

Health economic alternative hypothesis:
A 6 month diet and exercise program will be cost-effective when compared to an exercise only program at 12 months in people with hip OA.

Section 3: Trial Methods

9. Trial design

The ECHO trial is designed as a two-arm, pragmatic-superiority parallel-design randomized controlled trial. Treatment allocation is a 1:1 ratio.

10. Randomisation

Participants will undergo 1:1 randomization into one of two groups: i) diet and exercise; or ii) exercise only. Computer-generated randomization was prepared by an independent biostatistician. Participants will be first randomly allocated to one of the two groups in a 1:1 ratio, using permuted blocks of varying sizes stratified by site (Melbourne or Sydney) and sex (male or female). Those who select "prefer not to say/other" will be randomised into either the male or female strata via toss of a coin. Participants will then be randomly allocated to a physiotherapist and if assigned to the diet and exercise group, further randomly allocated to a dietitian. The randomization schedule is stored on a password-protected website (REDCap™) at the University of Melbourne and maintained by a researcher not involved in participant recruitment or assessment. Group allocation is revealed to the participant by a researcher involved in neither the schedule preparation nor the concealment after baseline assessment has been completed.

11. Sample size

The primary outcome is the 6 month change in average hip pain severity in the last week measured using an 11-point numeric rating scale (0= 'no pain', 10= 'worst pain possible'); We aim to detect a minimal clinically important difference (MCID) between groups of 1.8 NRS units in change in average hip pain severity (baseline minus 6 months)[13]. We have performed the sample size calculation taking into account differential clustering between groups. As the physiotherapists treat participants in both groups, only the clustering by dietitians was accounted for in the sample size calculation. We have assumed a conservative standard deviation at baseline across all participants of 2.5 units and a conservative correlation between baseline and 6 month scores of 0.25, as guided by our other research[13]. We have also assumed an intra-cluster correlation of 0.05 and that there will be 5 dietitians treating approximately 8 patients each. Given these parameters, we need 40 per arm to achieve 80% power to detect the MCID in pain at a 0.05 significance level. Allowing for 20% attrition, we will recruit 50 participants per arm (n = 100 in total).

12. Framework

This trial uses a superiority hypothesis testing framework between groups for all outcomes.

13. Statistical Interim analyses and stopping guidance

Nil

14. Timing of final analysis

Final analysis will be performed after all participants have reached the 12 month timepoint and completed assessments.

15. Timing of outcome assessments

Table 4.6 in the study protocol details the timing of outcome assessments, the majority of which occur at baseline, 6 months and 12 months.

Section 4: Statistical Principles

16. Level of statistical significance

All applicable statistical tests will be two-sided and will be performed using a 5% significance level for the analysis of the primary outcome.

17. Description of any planned adjustment for multiplicity, and if so, including how the type 1 error is to be controlled

We have one primary outcome (hip pain) and multiple secondary outcomes (body weight, body mass index, visceral fat mass, total body fat mass, other measures of hip pain, physical function, quality of life, perceived change in hip problem and in physical activity). We will not adjust for multiplicity in the analysis of exploratory secondary outcomes but instead report all effect sizes, confidence intervals, and p values in order to let readers use their own judgement about the relative weight of the conclusions on the effect of adding a diet intervention to exercise for hip OA. This approach aligns with the usage of p-values favoured by the American Statistical Association[14].

18. Confidence intervals to be reported

All confidence intervals will be two-sided 95% confidence intervals.

19. Adherence and Protocol Deviations

The primary analysis will be based on the principle of intention-to-treat, whereby participants are included in the groups to which they were originally assigned, regardless of their adherence to their assigned treatments. Any protocol deviations (if they occur), including errors applying inclusion/exclusion criteria and/or administration of the wrong intervention will be summarised in trial results (participant flow diagram/text) by treatment group.

In this trial, participants are required to undertake a diet and exercise program or an exercise only program. A number of adherence measures are being collected as outlined below. Data from all adherence measures will be reported using means, standard deviations and proportions (number and percentage) as appropriate for each treatment group:

Adherence	Description	Scale	Data collection time point
Self-rated adherence to physical activity plan	Self-reported on a 5-point Likert Scale for "How much of the time in the past 6 months did you follow your physical activity plan?"	Ranging from "none of the time"=0 to "all of the time"=4	6 months
Self-rated adherence to diet plan (diet and exercise group only)	Self-reported on a 5-point Likert Scale for "How much of the time in the past 6 months did you follow your diet plan as it was outlined by your study dietitian?"	Ranging from "none of the time"=0 to "all of the time"=4	6 months

Self-rated number of strengthening exercise sessions completed over the past 2 weeks	Self-reported in whole numbers.	Number	6 months
Number of consultations attended with physiotherapist	Physiotherapist consultation notes.	Range 0-5	Over first 6 months
Number of consultations attended with dietitian (diet and exercise group only)	Dietitian consultation notes.	Range 0-6	Over first 6 months
Number of weeks using meal replacements (diet and exercise group only)	Self-reported	Number	6 months

20. Analysis Populations

The primary analysis will be based on the principle of intention-to-treat, whereby participants are included in the groups to which they were originally randomised, regardless of their adherence to their assigned groups.

Section 5: Trial Population

21. Screening Data

Screening data will be collected and summarized. A CONSORT flow diagram will be used[15]. The following summaries will be presented in text and/or flow diagram: time frame for recruitment, the number of participants screened, the number of participants recruited, the number of screened participants not recruited, and the reasons for non-recruitment.

22. Eligibility

Inclusion criteria for participants are: (1) aged 50 years or older; (2) report a history of hip pain ≥3 months; (3) report an average pain score of at least 4 on an 11-point numeric rating scale (anchored at 0 = no pain, 10 = worst pain imaginable) over the previous week; (4) report pain in the groin or hip region on most days of the past month[16]; (5) have femoral or acetabular osteophytes and joint space narrowing (superior, axial and/or medial) on x-ray)[16]; (6) have access to a device with internet connection; (7) have a BMI > 27 kg/m^2; based on the Royal Australian College of General Practitioners guideline for obesity management, which indicates usage of a very low energy diet to induce rapid weight loss for those with BMI > 30 kg/m^2 or those with BMI > 27 kg/m^2 who also suffer comorbidities such as OA[17]; (8) are willing and able to give informed consent and participate fully in the interventions and assessment procedures; (9) have the ability to weigh themselves (e.g. access to scales); (10) pass the Exercise and Sports Science Australia stage 1 adult pre-exercise screening system[18] or obtain general practitioner clearance for participation in the study.

Participants are excluded from the study if they: (1) weigh > 150 kg (due to the added complexities of additional nutritional requirements for individuals above this weight); (2) are unable to speak and read English; (3) are on a waiting list for/planning back/lower limb surgery or bariatric surgery in the next 12 months; (4) have had previous arthroplasty on affected hip; (5) have had recent hip surgery on affected hip (past 6 months); (6) have self-reported inflammatory arthritis (e.g. rheumatoid arthritis); (7) lost > 2 kg weight over the previous 3 months (to ensure that participants were not already engaging in weight change behaviour); (8) are already actively trying to lose weight by any of the following mechanisms: a) using meal replacements for weight loss; b) being a member of a commercial weight loss program (e.g. Weight Watchers); c) receiving support from any health care professional for weight loss (i.e. participating in ongoing consultations about weight loss with a health care professional); d) using any drugs prescribed to aid in weight loss; e) using structured meal programs for weight loss such as 'Lite n' Easy'; (9) are unable to undertake a ketogenic VLCD without close medical supervision including self-reported: a) diagnosis of Type 1 diabetes; b) Type 2 diabetes requiring insulin or other medication apart from metformin; c) warfarin use; d) stroke or cardiac event in previous 6 months; e) unstable cardiovascular condition; f) fluid intake restriction; g) renal (kidney) problems (unless clearance is obtained from GP, including GP confirmation that estimated glomerular filtration rate > 30 mL/min/1.73m2); (10) have any neurological condition affecting lower limbs; (11) are pregnant or planning pregnancy; (12) have vegan dietary requirements (due to the complexity of delivering a nutritionally complete diet within the ketogenic diet regime).

In cases where an eligible participant reports bilateral hip pain, the most painful hip is considered the study hip.

Reasons for exclusion will be summarized in the CONSORT[15] flow diagram.

23. Recruitment

A CONSORT flow diagram[15] will be used to describe the number of people enrolled, randomized, allocated to each group, lost to follow up (including reasons) and analysed.

24. Withdrawal/follow-up

If a participant withdraws from the study, the nature, timing of and reasons for withdrawal will be described (provided the participant responds to contact made by the research team). Any data provided up to the point of withdrawal will be analysed in accordance with intention to treat analyses, unless the participant specifically requests to withdraw their data from the study. Losses to follow-up (including reasons) will be summarised in the CONSORT flow diagram by intervention group.

25. Baseline characteristics

Baseline characteristics will be summarised by intervention group and presented in a table:

- Age
- Sex
- Height
- Duration of hip symptoms
- Laterality of symptoms
- Geographical location
- Education level
- Current employment status
- Radiographic disease severity
- Co-morbidities
- Pain medication use
- Expectation of treatment outcome
- Problem in other joints

Baseline characteristics will be summarised as appropriate (means and standard deviations for continuous variables that appear to be distributed approximately symmetrically, medians and interquartile ranges for other continuous variables, counts and percentages for categorical variables). Tests of statistical significance will not be undertaken to compare baseline characteristics of intervention groups; rather, the clinical importance of any imbalance will be noted.

An appendix table will provide summaries of group allocation, baseline characteristics and baseline levels of primary and secondary outcomes between two groups: those participants who provide the primary outcome at 6 months, and those participants who are missing the primary outcome at 6 months (if >5% missing primary outcome data at 6 months).

Section 6: Analysis

26. Outcome definitions

Primary outcome:

- Change in average hip pain severity in the last week: Overall average hip pain severity in the last week is self-assessed via an 11-point NRS (0= 'no pain', 10= 'worst pain possible'). Change score at 6 months (primary time point) and 12 months (secondary time point) will be calculated as baseline minus follow-up.

Secondary outcomes:

- Change in body weight (kg). Change in body weight at 6 months and 12 months will be calculated as baseline minus follow-up.
- Change in body mass index (kg/m^2). Change in body mass index at 6 months and 12 months will be calculated as baseline minus follow-up.
- Change in visceral fat mass (g). Change in visceral fat mass at 6 months will be calculated as baseline minus follow-up.
- Change in total body fat mass (g). Change in total body fat mass at 6 months will be calculated as baseline minus follow-up.
- Change in hip pain, physical function, hip-related quality of life: Responses to the Pain (10-items), Activities of Daily Living (17-items) and Quality of Life (4-items) Subscales of the Hip Osteoarthritis Outcome Scale are provided on a 5-point Likert scale and scores range from 0 to 100, where higher scores represent better outcomes. Change of the score for each subscale at 6 months and 12 months will be calculated as baseline minus follow-up.
- Change in health-related quality-of-life: The AQoL-8D comprises 20 items that assess independent living, mental health, relationships, pain, coping and senses. Scores range from -0.04 to 1.00 with higher scores indicating better quality of life. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.
- Hip pain, as a binary variable of whether participants meet or exceed the minimal clinical importance difference (MCID) in average hip pain (1.8 NRS unit improvement) at 6 months and 12 months.
- Overall global change in hip problem at 6 and 12 months: This will be scored using a 7-point Likert scale. The terminal descriptors are 'much worse' to 'much better'. Participants reporting that they are 'moderately better' or 'much better' will be classified as 'improved'. All other respondents will be classified as not improved.
- Overall global change in physical activity at 6- and 12 months: This will be scored using a 7-point Likert scale. The terminal descriptors are 'much less' to 'much more'. Participants reporting that they do 'moderately more' or 'much more' will be classified as 'improved'. All other respondents will be classified as not improved.

27. Analysis methods

The statistical analysis plan will be published on the Centre for Health, Exercise and Sports Medicine's website while the biostatisticians (FM, supervised by ADS) are blinded to group details. We will conduct an intention-to-treat analysis whereby all participants will be included in the analysis in the group to which they were randomised. Analysis will be conducted by a biostatistician blinded to treatment group name, with two-sided hypothesis tests. If the proportion of missing data in the primary

outcome exceeds 5% at the primary timepoint of 6 months, missing outcome data will be imputed using multiple imputation methodology and multiply-imputed data will be used for the main analyses. For continuous outcomes, baseline, 6- and, where relevant, 12- month outcomes as well as changes from baseline (baseline minus 6 months and, where relevant, 12 months) will be summarised for each group as means with standard deviations. Counts and percentages of participants experiencing improvements based on global change scores and of participants achieving the MCID in improvement in pain (1.8 NRS units) will be reported in each treatment group at 6- and 12 months.

For the primary hypothesis, differences in mean change in average hip pain (baseline minus follow-up) will be compared between groups using a mixed-effects linear regression model including all data from 6 and 12 months for each participant with random effects for participants, and accounting for clustering by physiotherapist and dietitian as appropriate. The model will be adjusted for baseline values and the stratifying variables of site (Sydney/Melbourne) and sex (male/female). Results will be presented as mean differences in change between groups with two-sided 95% confidence intervals, and p-values will also be reported.

Similar mixed-effects linear regression models will be used for continuous secondary outcomes measured at baseline, 6 months, and 12 months. For continuous secondary outcomes measured at baseline and 6 months, between-group differences in mean change (baseline minus follow-up) will be compared using mixed-effects linear regression models adjusted for baseline values and the stratifying variables of site (Sydney/Melbourne) and sex (male/female), and accounting for clustering by physiotherapist and dietitian as appropriate. For the binary secondary outcomes, participants experiencing improvements based on global change scores and those achieving the MCID in improvement in pain (≥1.8 NRS units), groups will be compared using risk differences and risk ratios, calculated from logistic regression models including a term for time and an interaction between time and treatment group as covariates and adjusted for the stratifying variables of site (Sydney/Melbourne) and sex, and fit using generalized estimating equations to account for clustering. For all between-group comparisons, effect sizes, two-sided 95% confidence intervals and p-values will be reported. Standard diagnostic plots will be used to check model assumptions.

Exploratory analyses will be conducted using similar mixed-effects regression models as used for secondary continuous outcomes measured at baseline, 6 months and 12 months for the following measures:

- Total body lean mass in grams (at 6 months only)
- Depression, anxiety and stress at 6 months and 12 months
- Pain-related fear of movement at 6 months and 12 months
- Self-control for eating at 6 months and 12 months

Other measures will be summarised as appropriate, unless otherwise stated, by intervention group and presented in tables or summarised in text:

- Total body lean mass percentage at 6 months
- Total body fat mass percentage at 6 months
- Visceral fat mass percentage at 6 months
- Self-reported pain medication use at 6 months and 12 months
- Self-reported use of co-interventions at 6 months and 12 months
- Fidelity measures for intervention delivery by clinicians
- Health care use (for economic analyses conducted by health economist – see section 32)

28. Statistical Methods – adjustment for covariates

As described above, analyses of all continuous outcomes will be conducted adjusting for baseline value of the outcome as a covariate and the stratifying variables of site (Sydney/Melbourne) and sex (male/female).

29. Statistical Methods – sensitivity analyses

If multiple imputation is required to handle missing data, complete-case analyses will also be conducted in sensitivity analyses.

30. Statistical Methods – subgroup analyses

Pre-identified potential moderators include sex, expectation of treatment effects and baseline body mass index. Expectation of treatment effects will be dichotomized into "Benefit"=Moderate improvement, Large improvement and Complete recovery and "No benefit"= No effect at all and Minimal improvement. To assess the moderation of the effect of randomised treatment group on the primary outcome by the potential moderators, an interaction term between randomised group and the potential moderator, will be included in outcome regression models. Results will be calculated as the estimated treatment effect on the primary outcome separately for males and females, of an expectation of "benefit" and "no benefit" and of a one-unit increase in body mass index for each group at 6 months.

The hypothesis for each moderator analysis is below:

- Sex: Males in the diet and exercise group will report greater improvement in the primary outcome than females (relative to the exercise group).
- Expectation of treatment effects: Participants in the diet and exercise group who have an expectation of "benefit" from treatment effects will report greater improvement in the primary outcome than those who have an expectation of "no benefit" from treatment effects (relative to the exercise group).
- Body mass index: Participants in the diet and exercise group who have a higher BMI at baseline will report greater improvement in the primary outcome than those with a lower BMI (relative to the exercise group).

31. Missing data reporting and assumptions/statistical methods to handle missing data

An appendix table will provide summaries of group allocation, baseline characteristics and baseline levels of primary and secondary outcomes between two groups: those participants who provide the primary outcome at 6 months, and those participants who are missing the primary outcome at 6 months (if more than 5% of participants are missing the primary outcome at 6 months). If more than 5% of participants are missing the primary outcome at 6 months, multiple imputation will be applied. The number of imputed datasets will be approximately equal to the proportion of participants missing primary outcome data, with a minimum of 10 imputations conducted. Missing baseline characteristics will be imputed using single mean imputation. Missing outcome values at all relevant timepoints will be imputed separately by treatment group, using chained equations and predictive mean matching, using the five nearest neighbours [19]. Imputation models will include baseline levels of outcomes, age, sex, height, duration of hip symptoms, geographical location, education level, current employment status, problem in other joints, radiographic disease severity, number and type of co-morbidities and expectation of treatment pain medication use. Initially imputation models will include all primary and secondary outcomes together, with outcomes broken into subsets if imputation models do not converge. Imputed datasets will be compared to complete data using density plots for continuous outcomes and

descriptive tabulations for the binary outcomes. Estimates from the imputed datasets will be combined using Rubin's rules[20]. To assess the potential impact of the violation of the missing-at-random assumption on conclusions for the primary outcome, a pattern-mixture approach (as in White et al[21] will be applied.

32. Additional Analyses

The association between amount of weight lost at 6 months and change in pain at 6 months will be evaluated using a mixed-effects linear regression model including all data from 6 and 12 months for each participant with random effects for participants, and accounting for clustering by physiotherapist and dietitian as appropriate. The model will include a term for weight lost at 6 months (as a percentage of baseline weight) and be adjusted for baseline values of the outcome, treatment group allocated and the stratifying variables of site (Sydney/Melbourne) and sex. Demographic variables thought to affect both weight loss and pain aside from the stratifying variable of sex, including baseline weight and age, will also be included in the model. Results will be presented as the mean (95% confidence interval) change in pain for each percentage point increase in the amount of weight lost from baseline to 6 months.

A health economist (AH) will oversee a nested cost-utility analysis (separately to the afore-mentioned statistical analyses) taking the perspective of the Australian health care system using data from the main trial. Custom-developed surveys will collect self-reported information on frequency of visits to health care providers, use of prescription and over the counter medications, injections, hospitalisation and investigative procedures over 6 month intervals at baseline, 6 months and 12 months. Incremental cost-effectiveness will be calculated by taking a ratio of the between group difference in the mean costs and the mean utility over 12 months. QALYs over 12 months will be calculated from AQoL8D scores at 0, 6 and 12 months. Using a threshold value of $A70,000 per QALY, the net monetary value of the difference between groups over 12 months will be calculated. We will test that the incremental cost per additional QALY from the addition of the diet program to the exercise program is greater than the threshold willingness to pay for a QALY ($p<0.05$) and report the 90%CI for the incremental cost per additional QALY to correspond with the one sided alpha=0.05 test of the null hypothesis that net monetary benefit (NMB) is ≥ 0[22]. We will also plot a cost effectiveness acceptability curve as the one-sided NMB (1-alpha) values against levels of the threshold and interpret points on the plot line as our percent confidence in value for money of adding the diet program at each willingness to pay level.

33. Harms

Adverse events will be defined as any untoward medical occurrence, irrespective of whether it is related to the study interventions or not. Adverse events will be self-reported by participants at 6 and 12 months. Participants are requested to provide details on the nature of the event, if they sought treatment from a doctor or any other health professional, if the event was life-threatening or required hospitalisation, and whether they considered the event related to any component of the intervention they are receiving as part of the study. The Chief Investigator along with other study investigators will determine causality. If the event is related to the trial, it will be deemed a related adverse event. A serious adverse event will be defined as any untoward medical occurrence that; i) results in death; ii) is life-threatening; iii) requires hospitalisation or prolongation of existing inpatients hospitalisation; iv) results in persistent or significant disability or incapacity; v) is a congenital anomaly or birth defect, or; vi) any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed.

We will report by group:

- the number and proportion of participants that withdraw from the trial due to a related adverse event;
- the number and proportion of participants that experience one or more serious related adverse events and the number and proportion of participants experiencing each type;
- the number and proportion of participants that experience one or more non-serious related adverse events and the number and proportion of participants experiencing each type.

34. Statistical Software

Stata v18.0 will be used (StataCorp. 2023. *Stata Statistical Software: Release 18.* College Station, TX: StataCorp LLC.).

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Appendix 1

VARIABLES IN THE DATA SET

Name	Description	Scale	Time-points measured	Variable name in dataset
StudyID	ID of participant	ECHO-001- ECHO-101	NA	StudyID
Physiotherapist	Physiotherapist participant randomized to after baseline assessment complete	1,2,3,4,5,6,7,8.	Randomisation	Physio in "Physio allocation" file
Dietitian	Dietitian participant in Diet+Exercise group randomized to after baseline assessment complete	1,2,3,4,5	Randomisation	dietitian
Site	Site of participant	1=Melbourne, 2=Sydney	Baseline	Site
Study hip	Study hip of participant	1= left, 2 = right	Baseline	StudyHip
Group	Group participant randomized to after baseline assessment complete	Diet+Exercise vs Exercise group.	Randomisation	Group
Primary Outcome*				
Severity of average hip pain	Scored on an 11-point numerical rating scale (NRS) for average overall hip pain in the last week.	Ranges from 0 to 10; where 0=no pain and 10=worst pain possible.	Baseline, 6 months and 12 months	nrs_pain_0w nrs_pain_6m nrs_pain_12m
Secondary Outcomes*				
Body weight	Measured using home scales (self-reported)	Kilograms	Baseline, 6 and 12 months	Selfreportweight_0w Selfreportweight_6m Selfreportweight_12m
Body mass index	Calculated from self reported weight in kilograms at baseline, 6 or 12 months divided by the square of height (at baseline)	kg/m^2	Baseline, 6 months, 12 months	Selfreportweight_0w/(Height_0w)^2 =BMI_0w To be

	in metres			derived using baseline height: BMI _6m BMI_12m
Visceral fat mass	Dual energy x-ray absorptiometry	Grams and % of total body mass	Baseline and 6 months	Grams: Total_VFM_ 0w Total_VFM_ 6m % of total body mass: VFM_percen tage_0w= Total_VFM_ 0w/ Total_BM_0 w*100 VFM_percen tage_6m= Total_VFM_ 6m/ Total_BM_6 m*100
Total body fat mass	Dual energy x-ray absorptiometry	Grams and % of total body mass	Baseline and 6 months	Grams: Total_BFM_ 0w Total_BFM_ 6m % of total body mass: FM_percent age _0w = Total_BFM_ 0w/ Total_BM_0 w*100 FM_percent age_6m= Total_BFM_ 6m/ Total_BM_6 m*100

Hip Osteoarthritis Outcome Scale (HOOS) Pain Subscale	Scored using 10 questions regarding hip pain in the last week, with Likert response options ranging from never/no pain=0 to always/extreme pain=4.	Ranges from 0 to 40 and normalised to 0 – 100 scale (=100-(average of 10 questions)/4*100). Higher scores indicating less pain.	Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: hoos_p1 hoosp2 hoosp3 hoosp4 hoosp5 hoosp6 hoosp7 hoosp8 hoosp9 hoosp10
Hip Osteoarthritis Outcome Scale (HOOS) Activities of daily living	Scored using 17 questions regarding hip function in the last week, with Likert response options ranging from no dysfunction=0 to extreme dysfunction=4.	Ranges from 0 to 68 and normalised to 0 – 100 scale (100-(average of 17 questions))/4*100). Higher scores indicating less dysfunction.	Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: hoosa1 up to hoosa17
Hip Osteoarthritis Outcome Scale (HOOS) Quality of Life Subscale	Scored using 4 questions regarding quality of life in the last week, with Likert response options ranging from never/not at all/none =0 to constantly/ totally/ extremely/ extreme =4.	Ranges from 0 to 16 and normalised to 0 – 100 scale (100-(average of 4 questions))/4*100). Higher scores indicating better quality of life.	Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: hoosqol1 hoosqol2 hoosqol3 hoosqol4

Quality of life (AQoL-8D)	Scored from 35 questions regarding health-related quality of life in the last week (various response options).	Total score ranges from −0.04 to 1.00; higher scores indicate better quality of life; calculated using https://www.monash.edu/business/che/aqol/using-aqol/scoring AQoL-8D utility algorithms, STATA-8D, accessed 7th May, 2024 with edits:
		`g dvQ30 = 0 if Q30==1`
		`replace dvQ30=0.2779755 if Q30==2`
		`replace dvQ30=0.7484356 if Q30==3`
		`replace dvQ30=1if Q30==4`
		as only 4 responses to aqol_q6:
			Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: aqol_q1 up to aqol_q35

		(https://www.aqol.com.au/choice-of-aqol-instrument/58.html).		
Global rating of overall change in hip problem	Binary variable derived from score using a 7-point global rating of change Likert scale with response options ranging from “much worse”(=1) to “much better”(=7) when compared to baseline.	Participants indicating they are “moderately better”(=6) or “much better”(=7) will be classified as improved(=1). All other respondents will be classified as not improved(=0).	6 and 12 months	Binary variable, global_overall_6 and global_overall_12, derived from: gcs_overall_6m gcs_overall_12m
Global rating of change in physical activity	Binary variable derived from score using a 7-point global rating of change Likert scale with response options ranging from “much less”(=1) to “much more”(=7) when compared to baseline.	Participants indicating they are “moderately more”(=6) or “much more”(=7) will be classified as increased(=1). All other respondents will be classified as not increased(=0).	6 and 12 months	Binary variable, global_pain_6 and global_pain_12, derived from: gcs_changePA_6m gcs_changePA_12m
Hip pain improvement by 1.8 NRS units or more	Binary variable: 0 if not (Dnrs_pain <1.8 NRS unit improvement in overall pain), 1 if do meet or exceed the minimal clinical important difference in overall pain (Dnrs_pain >= 1.8 NRS unit improvement)	Proportion expressed as percentage relative to number of participants allocated to each group.	6 and 12 months	NRSimprove_6 NRSimprove_12 Derived from: Dnrs_pain_6 = nrs_pain_0w - nrs_pain_6m Dnrs_pain_12m = nrs_pain_0w - nrs_pain_12m
Other measures				
Total body lean mass	Dual energy x-ray absorptiometry	Grams and % of total body mass	Baseline and 6 months	Grams: Total_BLM_0

				w Total_BLM_6m % of total body mass: LM_percentage _0w = Total_BLM_0w/ Total_BM_0w*100 LM_percentage_6m= Total_BLM_6m/ Total_BM_6m*100
Depression, anxiety and stress[23]	DASS-21 will be used to measure each of depression, anxiety and stress. Responses range from 0 (did not apply to me) to 3 (applied to me very much or most of the time)	Each has range 0-42 with higher scores indicating higher levels of depression, anxiety or stress.	Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: DASS_anxiety = sum(dass2 dass4 dass7 dass9 dass15 dass19 dass20)*2 DASS_depression = sum(dass3 dass5 dass10 dass13 dass16 dass17 dass21)*2 DASS_stress = sum(dass1 dass6 dass8 dass11 dass12 dass14 dass18)*2

Pain-related fear[24]	Brief Fear of Movement Scale for Osteoarthritis – consists of 6 questions using a 4-point scale (range 1-4).	Scores range from 6 to 24, higher scores indicate greater fear of movement.	Baseline, 6 months and 12 months.	Each with suffix _0w, _6m, _12m: bfom= sum(bfoms1 bfoms2 bfoms3 bfoms4 bfoms5 bfoms6)
Self-efficacy for eating control [25]	Weight Efficacy Lifestyle (WEL) Questionnaire. Scored from 20 statements regarding eating control on a 10-point NRS where 0="Not confident at all that I can resist the desire to eat" and 9="Very confident that I can resist the desire to eat".	Total scores range from 0-180; higher scores indicate greater eating self-efficacy	Baseline, 6 and 12 months	Each with suffix _0w, _6m, _12m: welq_neg_emotions =sum(welq_1 welq_6 welq_11 welq_16) welq_availability =sum(welq_2 welq_7 welq_12 welq_17) welq_soc_pressure =sum(welq_3 welq_8 welq_13 welq_18) welq_phy_discomfort =sum(welq_4 welq_9 welq_14 welq_19) welq_pos_activities=sum(welq_5 welq_10 welq_15 welq_20) welq_total =

				sum(welq_neg_emotions welq_availability welq_soc_pressure welq_phy_discomfort welq_pos_activities)
Co-intervention use	Participants complete a custom-developed table of common co-interventions and report whether they have used them in the past 6 months. Cointerventions 1-10: Manual therapy Orthotics, arch supports or wedging in your shoes Heat/cold treatment Cortisone injections Platelet Rich Plasma (PRP) injections Visco-supplementation (injection of gel-like substances into the joint eg Synvisc) Hydrotherapy (eg warm water exercises) Acupuncture Arthroscopic surgery Hip joint replacement surgery	Participants who have used a co-intervention once in the past 6 months will be reported as a current user.	6, and 12 months	cointerventions_6m_1 to cointerventions_6m_10 cointerventions_12m_1 to cointerventions_12m_10
Medication use	Self-reported Participants will complete a table detailing a variety of pain and arthritis medications and supplements and will indicate if they have used them over the previous month. meds1 Oral anti-	Medication and supplements that were taken in the past month. Oral Opioid Medication (e.g. oxycodeine, morphine, ms-contin, oxycontin, kapanol) meds3 will be merged with Tramadol meds5. At 6- and 12 months participants will indicate if they	Baseline, 6, and 12 months	Each with suffix _0w, _6m, _12m: meds1 meds2 meds3 meds4 meds5 meds6 Each with suffix _6m,

	inflammatory tablets or capsules (eg. Voltaren, Nurofen, Celebrex, Mobic) meds2 Paracetamol or Paracetamol combinations (e.g. Panado, Panadol Osteo, Panadeine Forte) meds3 Oral Opioid Medication (e.g. oxycodeine, morphine, ms-contin, oxycontin, kapanol) meds4 Oral Corticosteroids (e.g. prednisolone, dexamethasone) meds5 Tramadol meds6 Topical anti-inflammatory gels or creams (e.g. Voltaren emulgel)	have taken the medication less often, same as before or more often: meds_freq1 Compared to the start of the study, are you taking oral anti-inflammatory tablets or capsules (eg. Voltaren, Nurofen, Celebrex, Mobic); meds_freq2 Compared to the start of the study, are you taking paracetamol or paracetamol combinations (e.g. Panado, Panadol Osteo, Panadeine Forte); meds_freq3 Compared to the start of the study, are you taking oral opioid medication (e.g. oxycodeine, morphine, ms-contin, oxycontin, kapanol)		_12m: meds_freq1 meds_freq2 meds_freq3
Adherence				
Number of consultations attended with physiotherapist	Physiotherapist consultation notes.	Range 0-5. Present n (%).	Over first 6 months	physio_attendance
Number of consultations attended with dietitian (diet and exercise group only)	Dietitian consultation notes.	Range 0-6. Present n (%).	Over first 6 months	dietitian_attendance
Self-rated number of strengthening exercise sessions completed over the past 2 weeks	Self-reported in whole numbers.	Number (0-21).	6 months	No_Strength Sessions
Self-rated adherence to physical activity plan	Self-reported on a 5-point Likert Scale for "How much of the time in the past 6 months did you follow your physical activity plan?"	Ranging from "none of the time"=0 to "all of the time"=4. Present n (%).	6 months	Follow_PAPlan
Self-rated adherence to diet plan (diet and exercise group	Self-reported on a 5-point Likert Scale for "How much of the time in the past 6	Ranging from "none of the time"=0 to "all of the time"=4. Present n (%).	6 months	Follow_Diet Plan

only)	months did you follow your diet plan as it was outlined by your study dietitian?"			
Number of weeks using meal replacements (diet and exercise group only)	Self-reported	Number (0 to 27 weeks)	6 months	Number_Weeks_MR
Fidelity				
Duration of consultations with physiotherapist	Physiotherapist consultation notes.	Ranges from 0 to 60 minutes for 1st consultation and 0 to 40 minutes thereafter. A higher score indicates longer consultation.	Over first 6 months	Duration_C1 To Duration_C5 will be renamed with physio suffix
Duration of consultations with dietitian (diet and exercise group only)	Dietitian consultation notes.	Ranges from 0 to 60 minutes for 1st consultation and 0 to 40 minutes thereafter. A higher score indicates longer consultation.	Over first 6 months	Duration_C1 To Duration_C5 will be renamed Duration_dietC1 to Duration_dietC5
Prescribed 4-6 strength exercises	Strengthening exercises prescribed in consultation 1	1=met fidelity requirements, DNA=did not attend, . = physio did not record anything in this section of treatment notes OR missing treatment notes		Ex_prescribed_C1
Progressed strength exercises	Strengthening exercises progressed in consultations 2-5	1=met fidelity requirements, DNA=did not attend, . = physio did not record anything in this section of treatment notes OR missing treatment notes		Ex_prescribed_C2 to C5
Discussed physical activity plan	Physical activity plan discussed in consultations 1-5	1=met fidelity requirements, DNA=did not attend, . = physio did not record anything in this section of treatment notes OR missing treatment notes		PA_plan_C1 to C5
Consultation 1				
Discussed the importance of, and agreed on, a weight loss goal of at least 10%	diet_f1			
Assessed participant's readiness to lose weight	diet_f2			

Checked whether the participant was agreeable to making some effort to lose weight	diet_f3
Checked the participant's confidence in completing their weight loss plan	diet_f4
Asked the participant to weigh themselves weekly and keep a record	diet_f5
Consultation 2	
Discussed the participant's weight loss progress since their previous consult	diet_f8
Discussed any obstacles/challenges/barriers that the participant faced	diet_f9
Consultation 3	
Discussed the participant's weight loss progress since their previous consult	diet_f15
Discussed any obstacles/challenges/barriers that the participant faced	diet_f16
Consultation 4	
Discussed the participant's weight loss progress since their previous consult	diet_f23
Discussed any obstacles/challenges/barriers that	diet_f24

the participant faced	
Consultation 5	
Discussed the participant's weight loss progress since their previous consult	diet_f30
Discussed any obstacles/challenges/barriers that the participant faced	diet_f31
Consultation 6	
Discussed the participant's weight loss progress since their previous consult	diet_f35
Discussed any obstacles/challenges/barriers that the participant faced	diet_f36
Elements included at some stage between consultations 2-6	
Discussed the transition phase from meal replacements to healthy eating	Dietitians were asked this question 5 times, because they could complete this element at any stage between consultations 2-6 (hence 5 variable names listed below). They needed to say yes once in order to meet fidelity requirements. diet_f10 diet_f17 diet_f25 diet_f32 diet_f37 If 1 of these 5 variables was a yes, this was a yes.

Discussed healthy eating behaviours associated with long-term weight maintenance	Dietitians were asked this question 5 times, because they could complete this element at any stage between consultations 2-6 (hence 5 variable names listed below). They needed to say yes once in order to meet fidelity requirements. diet_f11 diet_f18 diet_f26 diet_f33 diet_f38 If 1 of these 5 variables was a yes, this was a yes.			
Harms				
Adverse events	Reported by participants using survey questions.	The number and proportion of participants that withdraw from the trial due to a related adverse event; the number and proportion of participants that experience one or more serious related adverse events and their types; the number and proportion of participants that experience one or more non-serious related adverse events and their types.	6 and 12 months	adv_events_yn_6m ae1_nature_6m ae1_rx_6m ae1_serious_6m ae1_related_6m ae2_yn_6m
Baseline measures				
Age	Calculated from date of birth (DOB) to date randomised (Randomisationdate). Dates reported in MM/DD/YYYY	Reported in years, no rounding. Aged 50 years or older inclusion criteria	Baseline	Derived: age = Randomisationdate minus DOB
Sex	Sex at birth.	1=male, 2=female, 3=prefer not to say/other	Baseline	Sex
Height	Measured using stadiometer at clinics	Measured in metres	Baseline	Height_0w
Current employment status	Participants will report their current employment status using a categorical	The number and proportion of respondents for each category will be reported.	Baseline	Employment

	scale with response option 1 = Currently employed (casual, part-time or full-time), 2 = Retired (not due to health reasons), 3 = Unemployed/student, 4 = No paid job (homemaker, domestic duties, volunteer), 5 = Unable to work due to health reasons			
Education level	Participants will report their current education level using a categorical scale with response options 1 = Less than three years of high school, 2 = Three years or more of high school, 3 = Some education beyond high school, 4 = Completed tertiary or higher education	The number and proportion of respondents for each category will be reported.	Baseline	Education
Laterality of hip symptoms	Participant will self-report if their symptoms are in one (=2) or both hips (=1).	Reported as number and percentage	Baseline	bilat_unilat
Duration of hip symptoms in the study hip	Participants will self-report the total duration of time since their study hip symptoms began.	Reported in years.	Baseline	SymptomDuration
Co-morbid conditions	Self-administered comorbidity questionnaire[26]	The number and proportion of comorbidities will be reported, excluding osteoarthritis.	Baseline	heart_0w hbp_0w dep_0w anemia_0w ulcer_0w ra_0w diab_0w lung_0w cancer_0w back_0w kidney_0w liver_0w other_prob_0w

Radiographic disease severity of hip osteoarthritis	Rated from a non-weight bearing x-ray using the KL scale (2,3,4).	The number and proportion of participants with Grade 2 (mild disease severity), 3 (moderate disease) and Grade 4 (severe disease) will be reported.	Baseline	KL grade
Expectation of treatment outcome	Rated using a Likert scale (0=no effect at all, 1=minimal improvement, 2=moderate improvement, 3=large improvement, 4=complete recovery)	The number and proportion of participants selecting each response option will be reported. Expectation of treatment effects will be dichotomized into "Benefit"=Moderate improvement, Large improvement and Complete recovery and "No benefit"= No effect at all and Minimal improvement.	Baseline	Treatmentexpectation used to derive Treatexp_bin
Problems (pain, aching, discomfort or stiffness) in other joints	Self-reported as 0=no, 1=yes at each location.	The number and proportion of respondents for each pain location will be reported.	Baseline	other_joint_probs___1 = Hand/wrist other_joint_probs___2 = Neck other_joint_probs___3 = Back other_joint_probs___4 = Hip other_joint_probs___5 = Knee other_joint_probs___6 = Foot/ankle other_joint_probs___7 = Shoulder other_joint_probs___8 = Elbow
Geographical location	Based on residential postcode, in accordance with Australian Statistical Geography Standard. 1 "Major city" 2 "Inner regional" 3 "Outer regional" 4 "Remote" 5 "Very remote"	The number and proportion of respondents for each location will be reported.	Baseline	Geographical classification

Please note:
*Continuous outcomes are change in (baseline minus follow-up).

Appendix 2

DEFINITIONS OF DERIVED VARIABLES IN THE DATA SET

Variable in data set	**Unit**	**Calculation**	**Range**	**Better**	**Variable label in spreadsheet**
Age	Reported in years, no rounding.	Calculated from date of birth (DOB) to date randomised (Randomisationdate).	>=45 years	NA	Age
Body mass index	kg/m^2	Body mass in kilograms divided by the square of (in metres).	N/A	N/A	Selfreportweight_6m/ $(Height\_0w)^2$ =BMI_6m Selfreportweight_12m/ $(Height\_0w)^2$ =BMI_12m
Change in severity of overall average hip pain in the past week (primary outcome):	11-point numeric rating scale, higher is worse.	Change score at 6 months (primary time point) and 12 months (secondary time point) will be calculated as baseline minus follow-up.	-6 (inclusion criteria of >=4, so if rate 4 at baseline and 10 at follow-up then 4-10 = pain worse by 6 units) to 10.	Positive changes mean improved from baseline.	Dnrs_pain_6 Dnrs_pain_12
Change in body weight	Measured using home scales (self-	Kilograms. Change score at 6 months and 12 months will be calculated		Positive changes mean	Dmass6, Dmass12

	reported)	as baseline minus follow-up.		improved from baseline.	
Change in body mass index	Calculated from self reported weight in kilograms at baseline, 6 or 12 months divided by the square of height (at baseline) in metres	Change score at 6 months and 12 months will be calculated as baseline minus follow-up.		Positive changes mean improved from baseline.	Dbmi6, Dbmi12
Change in visceral fat mass	Dual energy x-ray absorptiom etry	Grams. Change score at 6 months will be calculated as baseline minus follow-up.		Positive changes mean improved from baseline.	DTotal_VFM_6
Change in total body fat mass	Dual energy x-ray absorptiom etry	Grams. Change score at 6 months will be calculated as baseline minus follow-up.		Positive changes mean improved from baseline.	DTotal_BFM_6
Change in total body lean mass	Dual energy x-ray absorptiom etry	Grams. Change score at 6 months will be calculated as baseline minus follow-up.		Negative changes mean improved from	DTotal_BLM_6

				baseline.	
Change in Hip Osteoarthritis Outcome Scale (HOOS) Pain Subscale	Scored using 10 questions regarding hip pain in the last week, with Likert response options ranging from never/no pain=0 to always/extreme pain=4.	Ranges from 0 to 40 and normalised to 0 – 100 scale (=100-(average of 10 questions)/4*100). Higher scores indicating less pain. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-100 to 100.	Negative changes mean improved from baseline.	Dhoosp_t_6 Dhoosp_t_12
Change in Hip Osteoarthritis Outcome Scale (HOOS) Activities of daily living	Scored using 17 questions regarding hip function in the last week, with Likert response options ranging from no dysfunction =0 to extreme	Ranges from 0 to 68 and normalised to 0 – 100 scale (100-(average of 17 questions))/4*100). Higher scores indicating less dysfunction. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-100 to 100.	Negative changes mean improved from baseline.	Dhoosa_t_6 Dhoosa_t_12

	dysfunction =4.				
Change in Hip Osteoarthritis Outcome Scale (HOOS) Quality of Life Subscale	Scored using 4 questions regarding quality of life in the last week, with Likert response options ranging from never/not at all/none =0 to constantly/ totally/ extremely/ extreme =4.	Ranges from 0 to 16 and normalised to 0 – 100 scale (100-(average of 4 questions))/4*100). Higher scores indicating better quality of life. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-100 to 100.	Negative changes mean improved from baseline.	Dhoosqol_t_6 Dhoosqol_t_12
Change in depression, anxiety and stress[23]	DASS-21 will be used to measure each of depression, anxiety and stress. Responses range from 0 (did not apply to	Each has range 0-42 with higher scores indicating higher levels of depression, anxiety or stress. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-42 to 42.	Positive changes mean improved from baseline.	Suffix 6 and 12 to: DDASS_anxiety_ DDASS_depressio n_ DDASS_stress_

	me) to 3 (applied to me very much or most of the time).				
Change in pain-related fear[24]	Brief Fear of Movement Scale for Osteoarthritis – consists of 6 questions using a 4-point scale (range 1-4).	Scores range from 6 to 24, higher scores indicate greater fear of movement. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-18 to 18.	Positive changes mean improved from baseline.	Dbfom_6 Dbfom_12
Change in Self-efficacy for eating control [25]	Weight Efficacy Lifestyle (WEL) Questionnaire. Scored from 20 statements regarding eating control on a 10-point NRS where 0="Not confident at all that I can resist the desire	Total scores range from 0-180; higher scores indicate greater eating self-efficacy. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-180 to 180.	Negative changes mean improved from baseline.	Dwelq_total_6 Dwelq_total_12

	to eat" and 9="Very confident that I can resist the desire to eat".				
Change in health-related quality of life:	The AQoL questionnaire (version AQoL-8D) measures health-related quality of life.	This is a 35-item questionnaire and scores range from -0.04 to 1.00 with 1.00 indicating full health-related quality of life. Change score at 6 months and 12 months will be calculated as baseline minus follow-up.	-1.04 to 1.04.	Negative changes mean improved from baseline.	Daqol_8D6 Daqol_8D12
Complete primary outcome (derived only if >5% missing primary outcome at primary timepoint)	0,1.	Those participants who provide the primary outcome at 6months will be coded as 1; and those participants who are missing the primary outcome at 6 months will be coded as 0.	N/A	N/A	complete
At least one problem in other joint	0,1	At least one of other_joint_probs___1 other_joint_probs___2 other_joint_probs___3 other_joint_probs___5 other_joint_probs___6 other_joint_probs___7 other_joint_probs___8	NA	NA	Atleastoneproblem
At least 1 comorbidity	0,1	At least one of heart_0w hbp_0w dep_0w	NA	NA	Atleastonecomobidity

		anemia_0w ulcer_0w ra_0w diab_0w lung_0w cancer_0w back_0w kidney_0w liver_0w other_prob_0w			
At least 1 treatment at 6 months and 12 months (each timepoint separately)	0,1	At least one of cointerventions_6m_1 to cointerventions_6m_10. For timepoints 12 months as well.	NA	NA	Atleastonetreatment_6 Atleastonetreatment_12
At least 1 medication at baseline, 6 months and 12 months (each timepoint separately)	0,1	At least one of meds_final1_0w meds_final2_0w meds_final3_0w meds_final4_0w meds_final5_0w. Same for 6 month and 12 month timepoints.	NA	NA	Atleastonemedication_0 Same for 6 month and 12 month timepoints.