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ORIGINAL RESEARCH

Long-term effectiveness of a lifestyle intervention for rheumatoid arthritis and osteoarthritis: 1-year follow-up of the 'Plants for Joints' randomised clinical trial

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ABSTRACT

Objectives In two randomised controlled trials, the Plants for Joints (PFJ) multidisciplinary lifestyle intervention reduced signs and symptoms of rheumatoid arthritis (RA), or metabolic syndrome-associated hip or knee osteoarthritis (MSOA) compared with usual care. The current study investigated long-term outcomes.

Methods After completion of two 16-week trials in people with (1) RA or (2) MSOA, control groups switched to the active PFJ intervention. At the end of the intervention, all participants were followed up in a 1-year observational extension study. Primary outcomes were 28-joint Disease Activity Score (DAS28) (RA) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (MSOA). Secondary outcomes included body composition, metabolic outcomes, medication changes and intervention adherence. An intention-to-treat analysis with a linear mixed model was used to analyse within-group changes.

Results 65 (84%) of 77 RA participants and 49 (77%) of 64 MSOA participants completed the extension study. The effects of the PFJ intervention were replicated in the original control groups and sustained within the RA group a year after intervention completion (mean DAS28 −0.9 points; p<0.001), while in the MSOA group mean WOMAC increased towards but remained well under the starting value (−7.8 points, p<0.001). Improvements in C-reactive protein, waist circumference (RA and MSOA); low-density lipoprotein cholesterol (RA); and weight, haemoglobin A1c, blood pressure (MSOA) were also sustained. Participants had a net decrease of medication, and intervention adherence was largely sustained.

Conclusions A year after the PFJ lifestyle intervention, improvements of disease activity and metabolic outcomes within RA and MSOA groups were largely sustained and related to sustained adherence, with a net decrease of medication.

Trial registration numbers NL7800, NL7801.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Unhealthy lifestyles increase the risk and severity of rheumatoid arthritis (RA) and metabolic syndrome-associated osteoarthritis (MSOA). In two randomised controlled trials, the 4-month Plants for Joints (PFJ) multidisciplinary lifestyle intervention significantly improved disease activity and metabolic health in people with RA or MSOA.

WHAT THIS STUDY ADDS

⇒ The 1-year extension study of the PFJ intervention shows improvements of disease activity and metabolic outcomes, as well as intervention adherence in people with RA or MSOA, were largely sustained, with a net decrease in medication use.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings support the potential use of the PFJ intervention, as an additional treatment option in people with RA or MSOA.

INTRODUCTION

Systemic chronic low-grade inflammation is a common driver of both rheumatoid arthritis (RA) and metabolic syndrome-associated osteoarthritis (MSOA), of which its triggers, physical inactivity, obesity, intestinal dysbiosis, poor diet, stress and disturbed sleep are targeted by the Plants for Joints (PFJ) lifestyle intervention.[1 2] Also, people with RA and MSOA have an increased risk of comorbidities, including cardiovascular disease, of which chronic inflammation also plays a role in their onset and progression.[2–4]

The PFJ randomised controlled trial (RCT) investigated the effect of a multidisciplinary

lifestyle intervention based on a whole food plant-based diet, physical activity and stress management in people with low to moderately active RA or hip and/or knee MSOA.[1] After the 4-month intervention, disease activity was significantly decreased in people with RA (mean 28-joint Disease Activity Score (DAS28) −0.9 point),[5] while those with MSOA had significantly less pain and stiffness and improved physical function (mean Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score −11 points) compared with a usual care control group.[6] Both RA and MSOA groups had improved metabolic outcomes, including weight, fat mass, haemoglobin A1c (HbA1c) and low-density lipoprotein (LDL) cholesterol.[5 6]

Improvements in health behaviour and status are not always maintained after a successful lifestyle intervention.[7] Therefore, all participants were followed up in an extension study after completing the intervention, including the control group who received the intervention after the trial. The objectives of the current study were to determine (1) the long-term outcomes of the lifestyle intervention on disease activity and metabolic health in RA and MSOA, (2) whether participants could taper or stop medication use postintervention and (3) whether adherence to the intervention is associated with long-term outcomes.

METHODS

Design

Two assessor-blind open-label RCTs compared the effect of a multidisciplinary lifestyle intervention to routine care in people with (1) RA or (2) MSOA between May 2019 and December 2021 at the Reade rehabilitation and rheumatology clinic in Amsterdam, the Netherlands.[1 5 6] During the RCT, visits took place at baseline, 2 and 4 months. After completing the RCT, those who were in the control group also started the lifestyle intervention following the same schedule. After completing the active intervention period, all participants were invited to take part in an observational extension study with measurements at 6 and 12 months.

Study protocols were prospectively registered (International Clinical Trial Registry Platform numbers NL7800 and NL7801) and published.[1] The study followed the Strengthening the Reporting of Observational Studies in Epidemiology statement guidelines[8] and European Alliance of Associations for Rheumatology (EULAR) recommendations for reporting of clinical trial extension studies.[9]

Patient and public involvement

Patient partners were involved in the design of the intervention including the selection of the lifestyle components and patient-reported outcome measures. After the trial, participants helped evaluate the intervention, disseminate the results to the public, and, in cocreation with the public, improve the intervention for future use.

Study sample

Sample size calculations were previously described.[1 5 6] People aged ≥18 years were included in the RCTs if they had (1) RA according to the American College of Rheumatology (ACR)/ EULAR 2010 criteria, with a low to moderate disease activity (2.6≤DAS28 ≤5.1) and stable treatment with or without disease-modifying antirheumatic drug (DMARDs) for ≤3 months[10 11] or (2) hip and/or knee OA according to the ACR clinical criteria and metabolic syndrome according to the National Cholesterol Education Programme criteria.[6 12–14] 89% of participants fulfilled ACR radiological criteria for OA, 47 (knee, 73%) and 50 (hip, 78%) participants had a Kellgren-Lawrence grade between 2 and 4.[6 12–15] People with a body mass index <18.5 kg/m^2, already following a plant-based diet, unwilling to quit smoking during study and pregnant women were excluded. In this study, results are shown separately for RA and MSOA but are combined in one report as the same intervention was used.

Intervention

Details of the PFJ intervention were previously published.[1 5 6] Briefly, participants received individual intakes with a registered dietitian and a physical therapist at the start of the intervention. During the 4-month intervention mixed groups of RA and MSOA, participants received theoretical and practical education about a whole food plant-based diet, physical activity, and sleep and stress management during 10 group meetings of 6–12 participants.[15–19] This included a calorie-unrestricted plant-based version of the Guidelines on Healthy Nutrition from the Health Council of the Netherlands,[18] personal physical activity goals in accordance with the Dutch physical activity guidelines (150 min/week moderate intense physical activity and 2 days/week musculoskeletal strengthening activities),[19] psychoeducation on the effects of psychological stress on health and stress management and coaching on sleep. Education was provided by registered dietitians, a physiotherapist, personal trainers and therapists with expertise in sleep and stress reduction. During the intervention, participants were facilitated with general information and videos, exercises for at home, fully elaborated weekly menus and daily supplementation with methylcobalamin (1500 µg) and cholecalciferol (50 µg). During the extension, study participants were encouraged to continue to adhere to the intervention's recommendations. Also, during this time, participants were offered monthly newsletters, crafted by registered dieticians, containing recipes, articles, podcasts and six adherence-promoting webinars, presented by the PFJ dieticians or physical therapist, on topics like sustainable weight loss, unprocessed foods, the gut microbiome and guided (mindfulness) exercises.

Primary and secondary outcomes

The primary outcome for RA was the mean change in DAS28 over time from the start of the intervention to

the end of the extension study. Swollen and tender joint counts were assessed by an independent research nurse. The primary outcome for MSOA was the WOMAC total score (range 0–96, best to worst) over the same time measured with digital questionnaires via the CASTOR electronic data capture system.[20]

Secondary outcomes included changes in DAS28 or WOMAC score during the intervention and within the extension study for the control groups, and within the extension study for all participants; RA only: DAS28 components, DAS28 change for seropositive and seronegative subgroups; MSOA only: WOMAC subscores; all participants: body weight, waist circumference; dual-energy X-ray absorptiometry: body composition and bone density; fasted blood samples: erythrocyte sedimentation rate, C-reactive protein (CRP), glucose, HbA1c, LDL, high-density lipoproteins, triglycerides; blood pressure; validated Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire: depression, fatigue, pain interference and physical function.[21]

Dietary intake was measured with 'MijnEetmeter', a validated digital food diary.[22] Participants were asked to complete the diary for at least 4 days, including a weekend day. A 2-day dietary recall was performed during measurements for participants having difficulty or not filling in the food diary themselves. Minutes of stress-reducing and physical activities in the past week were assessed with a digital questionnaire. Adverse events were recorded.

Medication changes

While DMARD medication was kept stable, where possible, during the 4-month intervention period, participants could make medication changes as required during the extension study. Medication use was recorded at each measurement. For RA, participants with a DAS28<2.6 received a protocol as a suggested approach to taper antirheumatic medication with their rheumatologist (online supplemental appendix 1). Changes in medication at the end of the extension study as compared with the start of the intervention were classified as 'increase', 'stable' or 'decrease'. An 'increase' in medication was defined as an added medication, increased dosage or shortened interval of medication use, a switch to a different medication due to insufficient effect or receiving one or more glucocorticoid injection(s) since the previous measurement. 'Stable' medication was classified as no change in dosage or interval, or a switch to a different medication due to side effects. A medication 'decrease' was defined as a decreased dosage, increased interval between doses or discontinuation. In a selection of RA participants (n=27, including all participants switching antirheumatic medications), (reasons for) changes in antirheumatic medications were adjudicated by an independent committee (two rheumatologists and one resident).

Adherence

Adherence was measured during the intervention and 6 and 12 months after completing the intervention with an adapted version of the Lifestyle Index Adherence Score developed by Ornish *et al*.[1 23] A score of 1.0 indicated 100% adherence, defined as attendance of all ten meetings during the intervention, stress-reducing activities 6 days per week for ten minutes per day, physical activity 5 days per week for 30 min per day and mean intake of ≥14 g fibre per 1000 kilocalories (kcal) and <10% saturated fatty acids of total kcal per day (energy%).

Statistical analysis

RA and MSOA participants were analysed separately. To assess differences between participants completing or dropping out of the 1-year extension study changes in DAS28 or WOMAC from start to end of the intervention were compared with an independent t-test (normally distributed data) or a Mann-Whitney test (skewed data).

Changes in primary and secondary outcomes at the end of the 1-year extension study were analysed with an intention-to-treat analysis with a linear mixed model to estimate the within-group change over time. In the models, time was treated as a categorical variable represented by dummy variables. For these analyses, the intervention and control groups were combined into one cohort all starting at month 0 indicating the start of the intervention (month 0 for the intervention group and month 4 for the control group). Additional linear mixed models were performed to estimate the within-group change in outcomes between the end of the intervention and extension study and within the control group during the intervention period. Analyses were performed for all participants combined and within subgroups of the RCTs control groups and participants who completed the extension study. The linear mixed models, with the ability to handle data missing at random, incorporated all available participant data until the point they were lost to follow-up, when applicable.

To assess the relationship between adherence to the lifestyle intervention and changes in DAS28 or WOMAC score, the Lifestyle Index Adherence Score, and its individual components (as tertiles), with dietary intake, physical and stress-relieving activity data measured 12 months after intervention completion, were included in the model as well as the interaction between the adherence variables and time. Medication changes are described with descriptive statistics.

All analyses were performed with R V.4.3.1 (2023-06-16) and p values<0.05 were considered statistically significant. For the interaction terms, a p<0.1 was considered statistically significant.

RESULTS

77 (93%) RA participants completed the original trial, 40 in the intervention and 37 in the control group. Following the trial, the control group also received the intervention, and 65 participants (84%) completed the extension study (figure 1A). Twelve participants withdrew from the extension study primarily due to busy

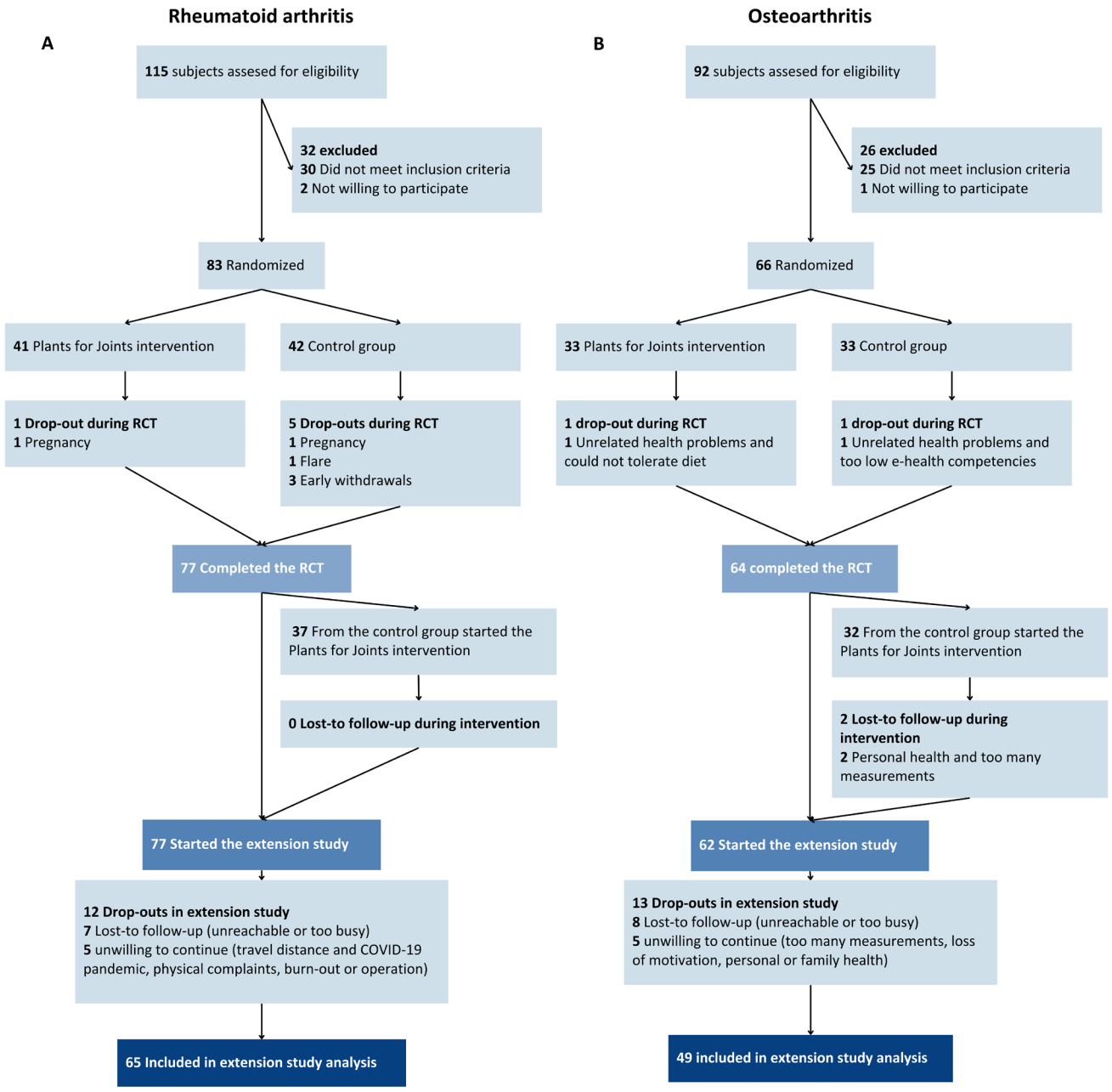

Figure 1 Strengthening the Reporting of Observational studies in Epidemiology flow diagram of (A) rheumatoid arthritis and (B) osteoarthritis participants in the Plants for Joints trial and 1-year extension study. RCT, randomised controlled trial.

schedules and numerous study measurements (mean post-intervention follow-up time of 10.4 months for all participants; figure 1A). Baseline characteristics and medication use are shown in table 1 and online supplemental table 1). Participants who completed the extension study had a lower DAS28 at the end of the intervention and a trend towards greater change during the intervention compared with dropouts (completer mean (SD) DAS28 at end: 2.94 (1.09), change: –1.0, drop-out DAS28 at end: 3.96 (1.61), change: –0.4).

64 (97%) MSOA participants completed the original trial, 32 in the intervention and 32 in the control group and 49 (77%) completed the extension study (figure 1B). Two participants from the control group dropped out before or during the intervention. Within the extension study, 13 participants dropped out primarily due to busy schedules and numerous study measurements (mean postintervention follow-up time of 10.0 months for all participants; figure 1B). Baseline characteristics and medication use are shown in table 2. During the extension study, six participants had a joint replacement surgery (knee n=3, hip n=3) and remained in the study (mean operation time point from start intervention was 11 months; mean preoperation WOMAC total score 34.8

Table 1 Characteristics of all RA participants at start intervention

Characteristic (n =)	77
Age, mean (SD), years	55 (12)
Female sex, no (%)	71 (92)
Body mass index, mean (SD), kg/m^2	26.3 (4.3)
Waist circumference, mean (SD), cm	91.0 (11.2)
Waist circumference, female, n=71	90.2 (11.1)
Waist circumference, male, n=6	100.3 (8.4)
Rheumatoid arthritis	
Disease duration, mean (SD), years	9.0 (8.4)
RF positive, no (%)	49 (64)
ACPA positive, no (%)	50 (65)
Seropositive, no (%)	57 (74)
DAS28, mean (SD)	3.85 (0.86)
Erosive disease, no (%)	37 (49)
Medication for RA, no (%)	
Methotrexate monotherapy	14 (18)
Methotrexate combination therapy	18 (23)
Other csDMARD monotherapy	4 (5)
Other csDMARD combination therapy	7 (9)
bDMARD monotherapy	11 (14)
tsDMARD monotherapy	3 (4)
Glucocorticoid monotherapy	3 (4)
No medication	17 (22)
Other medication, no (%)	
Pain	24 (31)
Antihypertensive	16 (21)
Cholesterol-lowering	8 (10)
Glucose-lowering	3 (4)

Data shown at the start of the intervention for both those who were randomised to the intervention group during the RCT and those who were initially in the control group and received the lifestyle intervention after completing the RCT.
ACPA, anticitrullinated protein antibody; bDMARD, biological DMARD; csDMARD, conventional synthetic DMARD; DAS28, 28-joint Disease Activity Score; DMARD, disease-modifying antirheumatic drug; RA, rheumatoid arthritis; RCT, randomised controlled trial; RF, rheumatoid factor; tsDMARD, targeted synthetic DMARD.

Table 2 Characteristics of all osteoarthritis (OA) participants at start intervention

Characteristic (n=)	64
Age, mean (SD), years	64 (6)
Female sex, no (%)	54 (84)
Body mass index, mean (SD), kg/m^2	33.3 (5.3)
Weight, mean (SD), kg	94.9 (15.9)
Waist circumference, mean (SD), cm	110.0 (12.9)
Waist circumference, female, n=54	108.9 (13.3)
Waist circumference, male, n=10	116.0 (8.9)
WOMAC total (range 0–96)	38.2 (16.2)
Location OA, no (%)	
Knee OA	25 (39)
Hip OA	12 (19)
Knee and hip OA	27 (42)
Metabolic syndrome-associated comorbidities, no (%)	
Hypertension	54 (82)
(Pre)diabetes type 2	12 (19)
Hyperlipidaemia	45 (70)
Medication use, no (%)	
Pain	24 (38)
Antihypertensive	41 (64)
Cholesterol lowering	24 (38)
Glucose lowering	13 (20)

Data shown at the start of the intervention for both those who were randomised to the intervention group during the RCT and those who were initially in the control group and received the lifestyle intervention after completing the RCT.
RCT, randomised controlled trial; WOMAC, The Western Ontario and McMaster Universities Osteoarthritis Index.

(23.2); postoperation 23.5 (9.9)). There was no significant difference between change in WOMAC total score during the intervention for participants who completed the extension study compared with dropouts (completer mean WOMAC at end: 27.0 (19.5), change: −10.0, drop-out WOMAC at end: 26.1 (16.2), change: −12.0).

Disease-related outcomes: RA

After completing the RCT, the control group received the lifestyle intervention, and while the initial change in DAS28 in the control group during the intervention (−0.5 (95% CI −0.8 to −0.1)) was smaller than the intervention group, a similar improvement was reached at the end of the extension study as compared with the start of the intervention (−0.8 (95% CI −1.2 to −0.5), figure 2A). For both groups combined, a within-group difference of −0.9 (95% CI −1.2 to −0.7) point was observed a year after the intervention compared with the start (p<0.001; figure 2B). Within the extension study the DAS28 improvement was maintained (−0.1 (95% CI −0.3 to 0.1)). All components of the DAS28 decreased significantly compared with before the intervention (table 3). The DAS28 decreased significantly in both seropositive and seronegative subgroups a year after the intervention compared with the start (−0.9 (95% CI −1.2 to −0.6) and −1.1 (95% CI −1.4 to −0.6), respectively) (online supplemental table 2). When assessing only those who completed the extension study, a similar within-group DAS28 change of −1.0 (95% CI −1.2 to −0.8) was found during the intervention compared with the whole population, and no change within the extension study (−0.1 (95% CI −0.3 to 0.1); p=0.4).

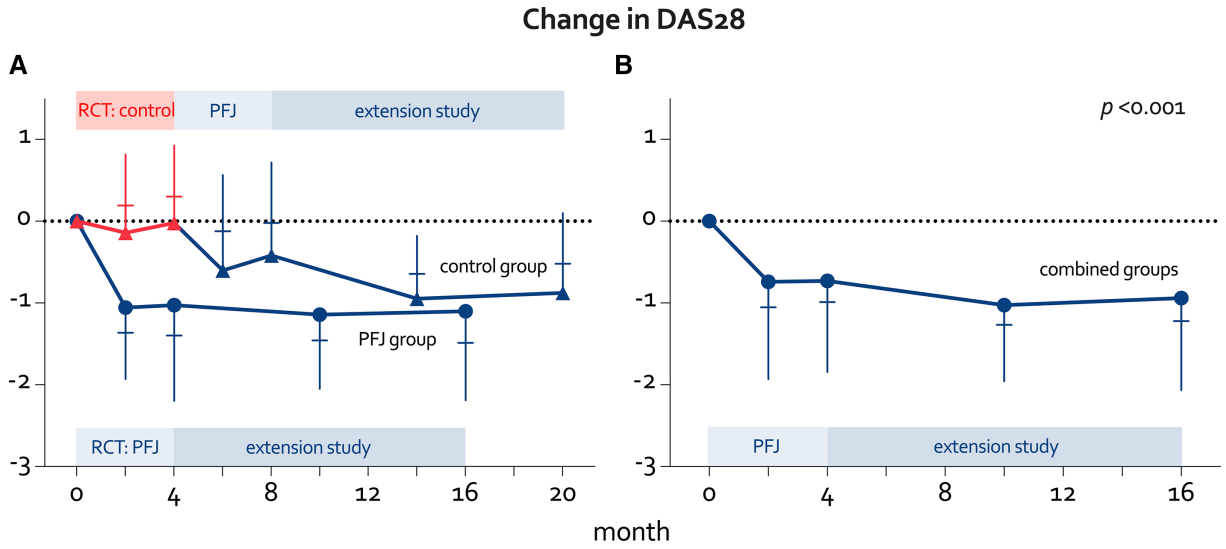

Figure 2 Mean change in DAS28 (A) per original trial arm and (B) for the whole cohort (all participants, data combined at start of active PFJ programme). Error bars represent 95% CI (horizontal) and SD (vertical). DAS28, 28-joint Disease Activity Score; PFJ, Plants for Joints; RCT, randomised controlled trial.

Disease-related outcomes: OA

Like the RA population, the initial WOMAC score change in the MSOA control group during the intervention (–7.8 (95% CI –12.5 to –3.2)) was smaller than in the intervention group, and this bridge was gapped 6 months after completing the intervention (figure 3A). Yet, while the WOMAC score increased again in the control group at the end of the extension study, the effects of the intervention were largely sustained for the intervention group (figure 3A). For both groups combined, in the year after completing the intervention the WOMAC score remained significantly lower as compared with the start of the intervention with a mean –7.8-point difference (95% CI –11.2 to –4.3; p<0.001) (figure 3B). Yet, within the extension study the WOMAC increased significantly as compared with the end of the intervention (3.5 (95% CI 0.2 to 6.7), p=0.04). All components of the WOMAC decreased significantly as compared with before the intervention (table 4). Excluding postoperation joint replacement surgery scores from the combined group statistical model yielded a smaller, but still significant improvement in the WOMAC total score of –6.4 (95% CI –9.7 to –3.1) compared with start intervention. Moreover, mean baseline WOMAC total score was lowest in participants with only knee OA (n=25; 34.3 (16.3)) compared with those with only hip OA (n=12; 40.6 (19.3)) or both knee and hip OA (n=27; 40.9 (14.5)). After the intervention, the WOMAC total score change was greatest in participants with both knee and hip OA (–14.5 (95% CI –18.9 to –10.1)) compared with those with only knee (–7.6 (95% CI –12.0 to –3.2)) or hip OA (–11.6 (95% CI –23.0 to –0.2)). At the end of the extension study, this trend was more pronounced: knee and hip OA: –12.9 (95% CI –17.7 to –8.1); only knee: –1.9 (95% CI –6.5 to 2.8)); only hip: –10.2 (95% CI –23.9 to 3.4). When assessing only those who completed the extension study, a similar within-group WOMAC score change of –8.2 (95% CI –11.8 to –4.6) was found during the intervention as compared with the whole population, yet there was no significant increase within the extension study (3.2 (95% CI –0.2 to 6.5); p=0.06).

Other outcomes: RA

A year after the intervention CRP, waist circumference and LDL cholesterol remained significantly lower than at the start (table 3), despite an increase in waist circumference (2.2 cm (95% CI 0.9 to 3.4)) and LDL cholesterol (0.2 mmol/L (95% CI 0.1 to 0.4)) within the extension study. During the extension study CRP decreased further by 0.5 mg/L as compared with the end of the intervention (p=0.03). While there was a significant reduction in weight and HbA1c at the end of the RCT for the intervention group as compared with the control group,[5] these changes were no longer found at the end of the extension study as compared with baseline (table 3). Furthermore, there was no significant change in lean mass, appendicular skeletal muscle mass (ASMM), bone density or patient-reported depression, fatigue, or physical function at the end of the extension study compared with the start of the intervention, yet participants reported significantly less pain interference (online supplemental table 2). Adverse events are described in online supplemental table 9.

Other outcomes: OA

For MSOA participants, CRP, weight, waist circumference, HbA1c, fasting blood glucose and blood pressure were significantly lower at the end of the extension study than at the start of the intervention (table 4), despite an increase in weight (1.6 kg (95% CI 0.1 to 3.0)) and HbA1c (0.9 mmol/mol (95% CI 0.1 to 1.7)) within the extension study. During the extension study, there was a reduction of systolic (–7 mm Hg (95% CI –13 to –1)) and diastolic blood pressure (–4 mm Hg (95% CI –7 to –2))

Table 3 Primary and secondary outcomes for combined groups of rheumatoid arthritis participants

	Intervention			Extension study		Within group	
	Start	Halfway	End	6 months	12 months		
n=	77	77	77	69	65	Difference (95% CI)	P value
DAS28 and components							
DAS28	3.85 (0.86)	3.00 (1.07)	3.09 (1.22)	2.79 (1.00)	2.84 (1.08)	–0.9 (–1.2 to –0.7)	<0.001
Swollen joint count of 28 joints	1 (0–3)	0 (0–2)	0 (0–2)	0 (0–1)	0 (0–1)	–1 (–2 to –0)	0.02
Tender joint count of 28 joints	3 (1–6)	1 (0–3)	1 (0–3)	1 (0–2)	1 (0–3)	–2 (–3 to –1)	<0.001
Patient global health, mm (0–100)	52 (36–64)	29 (14–50)	26 (10–44)	23 (7–45)	22 (4–36)	–24 (–30 to –19)	<0.001
ESR (mm/hour)	15 (7–26)	12 (7–26)	14 (7–27)	12 (5–21)	12 (5–24)	–3 (–5 to –1)*	0.02
DAS28<2.6, n (%)		22 (29)	29 (39)	28 (46)	25 (39)		
Inflammation							
C-reactive protein (mg/L)	2.4 (1.1–5.4)	2.7 (1.0–4.7)	2.1(0.7–5.2)	1.7 (0.7–3.7)	1.6 (0.7–2.9)	–1.0 (–1.8 to –0.5)*	0.005
Body composition							
Weight (kg)	74.5 (12.9)	72.2 (13.0)	71.5 (12.9)	73.1 (13.3)	74.6 (13.0)	–0.3 (–1.2 to 0.4)	0.5
Body mass index (kgm^{-2})	26.3 (4.3)	25.4 (4.3)	25.2 (4.4)	25.9 (4.6)	26.1 (4.3)	–0.1 (–0.4 to 0.2)	0.5
Waist circumference (cm)	91.0 (11.2)	88.0 (10.8)	87.6 (11.2)	89.0 (10.7)	89.8 (11.4)	–1.4 (–2.6 to –0.1)	0.03
Waist circumference (females)†	90.2 (11.1)	87.2 (10.7)	86.9 (11.1)	88.5 (10.5)	89.0 (11.4)	–1.2 (–2.6 to 0.1)	0.08
Waist circumference (males)†	100.3 (8.4)	96.6 (8.1)	96.2 (9.7)	96.8 (10.5)	97.3 (8.5)	–2.9 (–5.4 to –0.4)	0.03
Metabolic markers							
HbA1c (mmol/mol)	36.9 (6.4)	36.4 (6.7)	36.0 (6.0)	36.8 (6.7)	36.5 (7.0)	–0.3 (–0.9 to 0.2)	0.2
Fasting blood glucose (mmol/l)	5.1 (4.8–5.4)	4.9 (4.7–5.2)	4.9 (4.6–5.1)	5.1 (4.7–5.2)	4.9 (4.7–5.2)	–0.0 (–0.2 to 0.1)	0.7
LDL cholesterol (mmol/l)	3.1 (0.9)	2.6 (0.7)	2.7 (0.8)	2.8 (0.8)	2.9 (0.9)	–0.1 (–0.2 to 0.0)	0.04
HDL cholesterol (mmol/l)	1.6 (0.4)	1.5 (0.4)	1.6 (0.4)	1.6 (0.4)	1.7 (0.4)	0.0 (0.0 to 0.1)	0.2
Triglycerides (mmol/l)	1.1 (0.5)	1.1 (0.5)	1.0 (0.4)	1.0 (0.4)	1.0 (0.4)	–0.0 (–0.1 to 0.1)*	0.6
Systolic blood pressure (mm Hg)	134 (19)	130 (19)	128 (18)	133 (21)	134 (22)	0.7 (–2.5 to 3.8)	0.7
Diastolic blood pressure (mm Hg)	86 (11)	85 (11)	84 (11)	85 (17)	86 (12)	–0.4 (–3.1 to 2.2)	0.8

Outcomes at start and end of the 4-month intervention period as well as during the 1-year extension study (6 and 12 months after completing the intervention) for combined groups of participants taking part in the intervention during the RCT phase as well as the control group after the RCT. Continuous variables are reported as mean (SD) when normally distributed or as median (IQR) when skewed unless otherwise mentioned. Within-group differences were shown between start of the lifestyle intervention and end of the 12-month follow-up determined with the linear-mixed model when model assumptions were met. For variables in which model assumptions were not met

*a linear-mixed model was performed after log transformation and within group differences were reported as median difference of complete paired values determined with a Wilcoxon test (p values from the linear mixed model are shown, all were similar to the Wilcoxon test).

†Females n=71, males n=6.

DAS-28, 28-joint Disease Activity Score; ESR, erythrocyte sedimentation rate;HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RCT, randomised controlled trial;

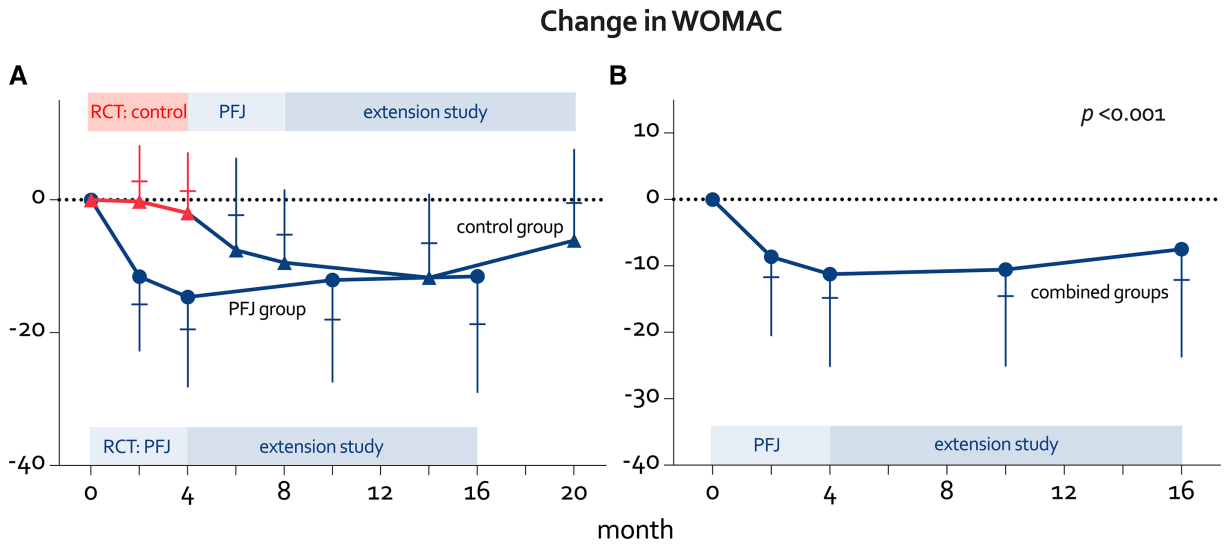

Figure 3 Mean change in WOMAC (A) per original trial arm and (B) for the whole cohort (all participants, data combined at start of active PFJ programme). Error bars represent 95% CI (horizontal) and SD (vertical). PFJ, Plants for Joints; RCT, randomised controlled trial; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

and no change in CRP, waist circumference, fasting blood glucose, and LDL cholesterol as compared with the end of the intervention. Furthermore, most of the observed weight loss was loss of fat mass (–2.5 kg (95% CI –1.8 to –0.4)), although there was a small, yet statistically significant, reduction in lean mass (–0.8 kg (95% CI –1.3 to –0.4)) and ASMM (–0.7 kg (95% CI –1.0 to –0.4)) (online supplemental table 3). Additionally, while there was a statistically significant decrease in bone density at the end of the extension period, the T-score remained in the healthy range (online supplemental table 3). Participants also had significant improvements of patient-reported fatigue, pain interference, and physical function, and no significant change in depression (online supplemental table 3). Adverse events are described in online supplemental table 9.

Medication changes: RA

Of the 56 (86%) RA participants who completed the extension study and used antirheumatic medications, 13 increased medication (23%, including 5 participants who started using medication), 15 kept medication stable (27%) and 28 (50%) decreased (n=18, 32%) or stopped one (n=5, 9%) or all antirheumatic medications (n=5, 9%)) (online supplemental table 4). The average dosage reduction of those with decreased medication intake was 62% (online supplemental figure 1). Furthermore, 45 participants (58% of medication users) had improved DAS28 scores (20 achieving DAS28<2.6) with stable or less antirheumatic medication at the end of the extension study as compared with the start of the intervention. Of those with a DAS28<2.6 at the previous measurement, 10 (34%) and 11 (39%) decreased their medication while 12 (41%) and 10 (36%) kept their medication stable, at 6 and 12 months after intervention completion, respectively.

Medication changes: OA

Of the 18 (37%) MSOA participants who completed the extension study and used pain medication, 4 (22%) increased, 2 (11%) kept stable and 12 (67%) decreased or stopped pain medication use (online supplemental table 4). Furthermore, 2 participants increased the use of either glucose-lowering or cholesterol-lowering medication, while 3 (33%) and 8 (44%) participants decreased these medications, respectively (online supplemental table 4).

Adherence

For both RA and MSOA groups, the median Lifestyle Adherence Score remained relatively stable from the end of the intervention to the end of the extension study (RA 1.05–0.99, MSOA 1.02–1.08, respectively) (online supplemental tables 6,7). The median intake of saturated fat (7–8 energy%, recommendation <10%) and fibre (21–22 g/1000 kcal, recommendation ≥14 g/1000 kcal) was within the healthy range at the end of the intervention and was sustained throughout the extension study (saturated fat: 8–9 energy%; fibre 19–21 g/1000 kcal) (online supplemental tables 6,7). Time spent on physical activity was in the recommended range at the start of the intervention for both RA and MSOA. At the end of the intervention, time spent per week on both physical and stress-relieving activities was increased as compared with the start, and these changes were sustained throughout the extension study (online supplemental tables 6,7).

A non-significant trend was found between higher adherence to the intervention and greater reduction of DAS28 or WOMAC score at the end of the extension study (figure 4, online supplemental table 8). Statistically significant decreases of DAS28 and WOMAC were found in all Lifestyle Index Adherence Score tertiles, except for

Table 4 Primary and secondary outcomes for combined groups of osteoarthritis participants

	Intervention			Extension study		Within group	
	Start	Halfway	End	6 months	12 months		
n=	64	63	62	58	49	Difference (95% CI)	P value
WOMAC score							
WOMAC total (0–96)	38.2 (16.2)	29.5 (18.0)	26.9 (18.9)	24.5 (16.7)	30.4 (18.6)	–7.8 (–11.2 to –4.3)	<0.001
WOMAC pain (0–20)	7.4 (3.0)	5.3 (3.4)	5.1 (3.7)	4.5 (3.4)	5.9 (3.7)	–1.5 (–2.3 to –0.7)	<0.001
WOMAC stiffness (0–8)	4.0 (1.8)	3.3 (1.8)	3.0 (2.0)	2.9 (1.7)	3.5 (2.2)	–0.5 (–1.0 to –0.1)	0.02
WOMAC physical function (0–68)	26.8 (12.8)	21.0 (13.7)	18.9 (14.0)	17.2 (12.2)	21.1 (13.7)	–5.7 (–8.3 to –3.1)	<0.001
Inflammation							
C-reactive protein (mg/L)	1.9 (1.0–4.5)	1.5 (1.0–3.2)	1.3 (0.8–3.0)	1.3 (0.8–2.2)	1.4 (0.9–3.3)	–0.7 (–1.4 to –0.2)*	0.009
Body composition							
Weight (kg)	94.9 (15.9)	92.2 (15.4)	90.2 (14.9)	90.7 (13.2)	93.9 (14.3)	–3.7 (–5.1 to –2.2)	<0.001
Body mass index (kgm^{-2})	33.3 (5.3)	32.5 (5.1)	31.7 (5.0)	31.5 (3.9)	32.9 (5.3)	–1.3 (–1.7 to –0.8)	<0.001
Waist circumference (cm)	110.0 (12.9)	105.9 (13.3)	104.6 (12.3)	105.7 (11.5)	107.4 (11.4)	–4.3 (–6.1 to –2.4)	<0.001
Waist circumference (females)†	108.9 (13.3)	104.7 (13.4)	103.3 (12.5)	104.6 (12.0)	107.2 (11.8)	–3.3 (–5.3 to –1.3)	0.001
Waist circumference (males)†	116.0 (8.9)	113.3 (9.9)	112.6 (7.7)	110.7 (7.3)	108.8 (10.2)	–9.2 (–14.2 to –4.1)	0.001
Metabolic markers							
HbA1c (mmol/mol)	42.6 (8.4)	40.7 (6.8)	40.3 (7.2)	40.2 (7.5)	40.5 (7.2)	–1.2 (–2.0 to –0.4)	0.003
Fasting blood glucose (mmol/l)	5.8 (5.3–6.5)	5.5 (5.1–6.0)	5.5 (5.1–6.2)	5.4 (5.1–5.9)	5.3 (4.9–6.0)	–0.4 (–0.6 to –0.2)	<0.001
LDL cholesterol (mmol/l)	3.6 (1.3)	3.2 (1.1)	3.3 (1.2)	3.3 (1.4)	3.6 (1.0)	–0.1 (–0.3 to 0.2)	0.7
HDL cholesterol (mmol/l)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.3)	0.0 (0.0 to 0.1)	0.4
Triglycerides (mmol/l)	1.6 (1.2–2.2)	1.4 (1.0–2.2)	1.6 (1.0–2.1)	1.5 (1.1–2.1)	1.4 (1.1–1.9)	–0.1 (–0.3 to 0.0)*	0.1
Systolic blood pressure (mm Hg)	145 (18)	141 (16)	144 (19)	142 (16)	136 (20)	–8 (–13 to –3)	0.005
Diastolic blood pressure (mm Hg)	91 (11)	86 (8)	89 (11)	86 (8)	85 (9)	–6 (–9 to –3)	<0.001

Outcomes at start and end of the 4-month intervention period as well as during the 1-year extension study (6 and 12 months after completing the intervention) for combined groups of participants taking part in the intervention during the RCT phase as well as the control group after the RCT. Continuous variables are reported as mean (SD) when normally distributed or as median (IQR) when skewed. Within-group differences were shown between start of the lifestyle intervention and end of the 12-month follow-up determined with the linear-mixed model when model assumptions were met. For variables in which model assumptions were not met

*a linear-mixed model was performed after log transformation and within group differences were reported as median difference of complete paired values determined with a Wilcoxon test (p values from the linear mixed model are shown, all were similar to the Wilcoxon test).

†Females n=54, males n=10.

HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RCT, randomised controlled trial; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

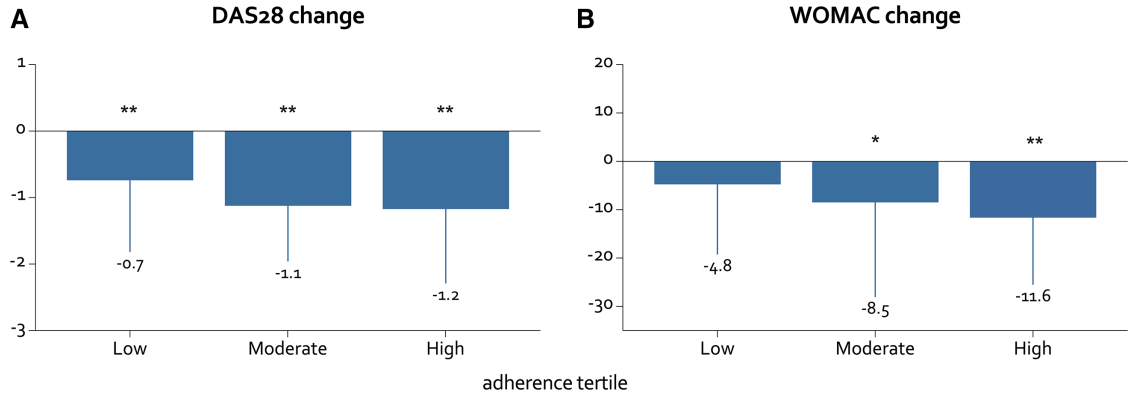

Figure 4 Mean change in DAS28 for people with rheumatoid arthritis (A) and WOMAC score for people with osteoarthritis (B) per tertile of the Lifestyle Index Adherence score. Tertile cut-offs for rheumatoid arthritis: <0.83=low, ≥0.83 and <1.13=moderate, ≥1.13=high; tertile cut-offs for osteoarthritis: <0.93=low, ≥0.93 and <1.20=moderate, ≥1.20=high. To assess the effect of adherence to the lifestyle programme on the change over time in the primary outcome variables (ie, DAS28 and WOMAC score), the Lifestyle Index Adherence Score, measured 12 months after programme completion, was included in a linear mixed model analysing within-group change over time as well as the interaction between the adherence variable and time. A p<0.1 was considered statistically significant. There was no significant difference found between tertiles. *p<0.1, **p<0.001. DAS28, 28-joint Disease Activity Score; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

the lowest tertile in MSOA participants (figure 4, online supplemental table 8).

DISCUSSION

A year after completing the PFJ intervention, in the RA group the DAS28 remained significantly lower than the start of the intervention, while in the MSOA group the WOMAC score increased towards but also remained significantly under the starting value. Also, the effects of the RCT were largely replicated in the RA and MSOA control groups, who received the intervention after completing the RCTs. Furthermore, CRP and metabolic outcomes, including waist circumference, fat mass, LDL cholesterol (RA only), and HbA1c and blood pressure (MSOA only), were significantly lower than at the start of the intervention. These results were obtained while (over) half of RA and MSOA participants using anti-rheumatic or pain medication, respectively, had a net decrease in medication use. Furthermore, participants remained largely adherent to the intervention, whereby trends towards a greater change in primary outcomes with higher adherence to the intervention were found.

For RA participants, the DAS28 reduction achieved during the intervention and sustained within the extension study surpassed the minimal clinically important difference target of 0.8, selected based on the range of our inclusion criteria of DAS28 (2.6 ≤DAS28 ≤5.1),[24] and is comparable to what is typically achieved in drug trials.[25] While a recent systematic review and meta-analysis reported no effects of varying dietary interventions, including vegetarian and vegan diets, on disease-related outcomes,[26] primarily due to small numbers of studies with small sample sizes, more recent studies support the short-term effects of plant-based dietary interventions in people with RA.[5 27 28] While only two studies have reported longer-term results, demonstrating the effectiveness of plant-based interventions which lasted 1 year,[29 30] this study further supports the long-term effectiveness of plant-based lifestyle interventions for people with RA.

For MSOA participants, the WOMAC score remained significantly lower a year after intervention completion compared with the start and exceeded the minimal clinically important difference of 20% for pain and physical function.[31] These findings are in line with an earlier intervention with a low-energy diet and physical activity which yielded similar short-term effects at 6 months to the PFJ RCT.[32] Despite a longer intervention duration (18 months) and extension study (3.5 years), similar within-group effects were also found at the end of the extension study compared with the PFJ extension study for WOMAC pain and function.[33] Conversely, within the PFJ extension study, the WOMAC increased again significantly as compared with the end of the intervention. This could be explained by a lower adherence to the intervention, although not supported by our adherence data. Yet, potential under-reporting cannot be dismissed as adherence data were self-reported and people that are overweight or obese have been shown to under-report nutritional intake.[34] Furthermore, participants with only hip or both knee and hip OA showed greater WOMAC total score improvements postintervention and in the extension study, compared with those with only knee OA. This could be explained by the lower baseline WOMAC score in the knee OA group, leaving less room for improvement. Yet, caution is needed in interpreting these findings due to small sample sizes.

Improvements in weight and HbA1c observed during the RCT in RA participants were not maintained at the end of the extension study, yet they had a healthier weight compared with the MSOA population and normal baseline HbA1c levels.[5] Still, waist circumference and LDL cholesterol remained significantly lower at the end of the

extension study, of importance for cardiovascular disease prevention.[3] Contrarily, MSOA participants sustained significant weight loss, of which primarily fat mass, at the end of the extension study comparable to a meta-analysis in people with overweight and obesity 1 year after lifestyle interventions (PFJ −3.7 vs −3.6 kg).[35] Apart from LDL cholesterol, metabolic changes remained significantly improved, including waist circumference, HbA1c and blood pressure. Overall, both RA and MSOA populations largely sustained metabolic effects a year after intervention completion, yet these effects were less pronounced than at the end of the intervention potentially due to attenuated adherence.

After completing the intervention, participants with RA and a DAS28 score <2.6 were given the option to taper antirheumatic medication. While 23% had increased their medication use, 50% of RA participants using antirheumatic medication decreased or stopped medication use. Yet, as 36%–41% of participants kept their medication stable, despite reaching a DAS28<2.6 at the previous measurement, potentially even more could have tapered their medication. Furthermore, given the side effects and costs associated with various DMARDs,[36 37] of which mean dosages decreased by 62%, the PFJ intervention also potentially contributes to reduced side effects and healthcare costs.

Various mechanisms may have contributed to the sustained, clinically relevant results found after the PFJ intervention. High-fibre intake is thought to protect the gut and reduce systemic inflammation associated with RA and OA aetiology and progression, through modifications of the gut microbiome and gut barrier integrity.[2 38 39] Ongoing studies into gut barrier integrity, microbiome and metabolomic testing in PFJ participants aim to further investigate these hypotheses. Whole-food plant-based foods also have lower caloric density, contributing to weight loss and satiety, and are naturally lower in saturated fat thus reducing cardiovascular risk.[40 41] Additionally, the synergistic effects of combining lifestyle interventions may have increased the programme's effectiveness compared with individual lifestyle components.[32]

Moreover, adherence to the intervention was largely sustained 1 year after the intervention, and relatively low drop-out rates (RA 16% and MSOA 24%) indicate good intervention acceptability. As low adherence and acceptability are often thought of as a concern when using plant-based dietary interventions, these findings, in addition to the outcomes of a process evaluation of the PFJ intervention (unpublished data), support the sustainability and acceptability of plant-based diets also found in other studies.[42 43] Psychological aspects of the programme, such as self-monitoring, social support and an emphasis on long-term changes without striving for perfection were found to contribute to the intervention's feasibility and acceptability (process evaluation to be published separately). These factors also contribute to (long-term) programme adherence, of importance as a non-significant dose-response trend was found between adherence and clinical improvements, consistent with similar studies in heart disease or obesity.[15 44]

Strengths of the study include the long-term assessment of effectiveness, medication changes and adherence. Limitations include the lack of a control group during the extension study, limiting internal validity and self-reported adherence data.[45] Also, the long-term effect of the intervention on DAS28 score is potentially overestimated due to data lost from RA participants who dropped out of the extension study. On the other hand, reductions of antirheumatic medication potentially downplay the effect of the intervention on DAS28. Moreover, six MSOA participants underwent joint replacement surgery during the study. These participants improved their mean WOMAC score from presurgery to postsurgery during the study. Excluding these participants from the statistical analysis, resulted in a smaller overall improvement in WOMAC score compared with including them, although still significant. Lastly, due to the multidisciplinary nature, singling out lifestyle components' effects is impossible.

CONCLUSION

In conclusion, a year after completing the PFJ intervention, disease activity in people with RA and pain, stiffness, and physical function in people with MSOA were significantly improved compared with the start of the intervention with a net decrease in antirheumatic or pain medication, respectively. The effects of the PFJ intervention were sustained within the RA group up to a year after intervention completion, yet in the MSOA group the WOMAC score regressed towards but remained under the starting value. Metabolic benefits found after the lifestyle intervention and adherence were also largely sustained at the end of the extension study. These results further emphasise the potential use of the PFJ intervention as an additional treatment option in people with RA or OA, alongside usual care.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the Medical Ethical Committee of the Amsterdam University Medical Centers approved the study protocol (EudraCT number NL66649.048.18). Participants gave informed consent to participate in the study before taking part.

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