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ORIGINAL RESEARCH

Self-evidence-based digital care programme improves health-related quality of life in adults with a variety of autoimmune diseases and long COVID: a retrospective study

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ABSTRACT

Objective To retrospectively investigate the feasibility and impact on health-related quality of life (HRQoL) of a digital care programme (DCP) designed to guide personalised diet and integrative interventions in a variety of autoimmune diseases and long COVID.

Methods Adults who participated in the DCP between April 2020 and June 2022, and for whom baseline (BL) and end-of-programme (EOP) Patient-Reported Outcomes Measurement Information System (PROMIS) scores were available, were included in this retrospective study. Changes from BL to EOP were calculated using standardised T-scores.

Results Two hundred two adults between 17 and 82 years old were included. Diagnoses included: rheumatoid arthritis (20.1%); long COVID (14.9%); psoriatic arthritis (10.9%); psoriasis (8.9%); systemic lupus erythematosus (6.4%); inflammatory bowel disease (5.9%); multiple sclerosis (5.9%); ankylosing spondylitis (5.4%) and other (23.3%). On average, individuals entered observations 7.6 times/day on 86% of programme days, attended 14 coach sessions and completed the programme in an average of 17.2 weeks. Statistically significant improvements were seen in all 10 PROMIS domains analysed. Individuals with higher severity of compromise at BL experienced greater average improvements than all-comers in all 10 PROMIS domains included.

Conclusion An evidence-based DCP that uses patient data to help identify hidden symptom triggers and guide personalised dietary and other non-pharmacological interventions was associated with a high level of engagement and adherence and statistically significant, clinically meaningful improvements in HRQoL. Those with the least favourable PROMIS scores at BL experienced the greatest improvements.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The human exposome (diet, lifestyle and environmental factors) is now recognised as having profound impacts on autoimmune disease (AID) onset and activity.

⇒ The complexity and heterogeneity of AIDs have impeded the development of uniform dietary and behaviour recommendations that are universally beneficial.

WHAT THIS STUDY ADDS

⇒ We found that a digital care programme which designs personalised trials ('N-of-1' trials) and relies on self-evidence to: (1) identify correlations between each patient's unique symptoms and sensitivities to their modifiable and non-modifiable exposome, and (2) educate and support patients in the iterative experimentation process required to adapt around triggers and use their own data to predict, lower and control symptoms, was associated with clinically meaningful improvements in health-related quality of life (HRQoL) across multiple domains in adults with AIDs, AID-associated conditions and long COVID.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings should prompt further investigation into the utility of personalised trials to optimise the success of non-pharmacological interventions in alleviating symptoms and improving HRQoL in patients with AID.

Autoimmune diseases (AIDs), a collection of more than 80 incurable chronic illnesses which have in common loss of self-tolerance and immune system attack on healthy tissues, are responsible for substantial morbidity and mortality worldwide. In 2005, the National Institutes of Health (NIH) estimated that 23.5 million Americans suffered from one or more AIDs.[1] As the prevalence of antinuclear antibody positivity in the USA was shown to be steadily increasing from the late 1980s through 2012,[2] that number has

likely increased domestically, and experts estimate that cases will continue to grow by 3%–9% annually across the globe.[3] Although the development of new drugs over the past two decades has decreased death rates and improved overall care, many patients with AID (even those receiving state-of-the-art treatment) are left coping with unpredictable and debilitating symptoms. In multiple studies across varying diagnoses, AIDs have been shown to have substantial negative impacts on health-related quality of life (HRQoL).[4] The emergence of long COVID, the symptoms of which mimic those of AID in many ways and is thought to have autoimmune origins in at least a subgroup-affected individuals, raises the number of people potentially suffering from autoimmune illness substantially.[5 6]

A growing body of research suggests that diet, lifestyle and a host of environmental factors have important influences on disease activity and HRQoL in AIDs and therefore may represent powerful yet underused opportunities for treatment.[7–16] In November 2022, the American College of Rheumatology released for the first time a clinical practice guideline for the integrative care of rheumatoid arthritis (RA).[17] Notably, all but one of the recommendations ('consistent engagement in exercise') were offered conditionally, highlighting the fact that, despite mounting evidence supporting complementary medicine's place in the treatment armamentarium for AID and a growing interest from patients, conclusive evidence about what constitutes a healthy autoimmune diet and lifestyle 'prescription' remains elusive. Rather than a lack of dietary and behaviour modification effectiveness, the reason for this may be a mismatch between traditional randomised controlled trial design and the inherent variability of responses of patients with AID to treatment and the complexity of their food and environmental sensitivities and interactions.[18] This variability and complexity, even within the same diagnosis group, are evidenced by considerable inconsistency in disease presentation, clinical course and response to pharmacological treatments. Therefore, it is proposed that classic trial designs, which typically examine uniform change in a single independent variable, are poorly suited to identify which interventions, among many possibilities, will be most effective in any individual patient with AID. Immune system responses and sensitivities are far too heterogeneous to expect that a statistically significant number of individuals with a certain diagnosis will react similarly to a uniform intervention, whether it be a drug, diet change or other lifestyle 'prescriptions'.

Therefore, the discovery of a truly effective diet and integrative intervention paradigm for AIDs, particularly in patients who have atypical triggers and multiple sensitivities, requires an innovative approach, one that incorporates evidence based on personalised ('N-of-1') trials and takes individual immune system sensitivities and reactivities and each patient's life circumstances into account. Support for the 'N-of-1' approach, especially as it relates to complex chronic diseases, is mounting and was the topic of recent special issue publications.[19 20] The digital care programme (DCP) reported on here is grounded in an 'N-of-1', a self-evidence-based approach.

This DCP relies on an individual's self-reported, digitally tracked data (obtained via an adaptive mobile application (app)) and weekly remote health coaching to inform highly personalised diet and lifestyle interventions which are monitored for efficacy and risks based on symptom response. It was previously studied in a randomised controlled pilot trial of 50 individuals with systemic lupus erythematosus (SLE) and showed statistically significant improvements in numerous HRQoL domains, including fatigue, pain intensity, pain interference, physical health and burden to others.[21]

The current retrospective study was undertaken to assess the feasibility of the DCP and to analyse changes in HRQoL following completion of the programme in individuals with a variety of AIDs, AID-related conditions and long COVID.

STUDY SUBJECTS AND METHODS

Study subjects

Patients who participated in the DCP between April 2020 and June 2022 and for whom baseline (BL) and end-of-programme (EOP) Patient-Reported Outcomes Measurement Information System (PROMIS) scores were available were included. Participants came to the programme via multiple sources: as a covered benefit through their insurance plan or employer, physician referral, peer referral or direct marketing. While patients were not involved in the design of this study, the programme is inherently patient-centric—each participant defined their own goals, in collaboration with their assigned health coach, at the beginning of their programme.

Survey data and measures

An intake form was administered prior to each individual's start of the DCP. It collected voluntary, self-reported background information including autoimmune and other diagnoses, weight, medications, race/ethnicity, education, marital status, employment and income. The form also inquired about the individual's ongoing symptoms which informed initial symptom tracking in the mobile app. At the conclusion of the programme, individuals were again asked to report current weight, symptoms and medications.

Patient-Reported Outcomes Measurement Information System

PROMIS is an NIH-supported set of validated measures designed to assess and monitor physical, mental and social aspects that impact HRQoL. The tools used in this study, the PROMIS 29+2 and the PROMIS short form V.1.0 Self-efficacy for Managing Chronic Conditions-Managing Symptoms 4a (henceforth referred to as PROMIS29+MSx), assessed 10 HRQoL domains: ability to participate in social roles and activities, cognitive function, ability to manage symptoms, physical function, anxiety, depression, fatigue, pain interference, pain

intensity and sleep disturbance. Each domain consists of a series of questions that were reported as T-scores standardised to a population mean±SD (50±10). Minimal important change (MIC) was established by domain using descriptive statistics (mean and SD in T-scores) to define thresholds 0.5 SDs from the mean.

Feasibility: tracking and health coaching adherence

Feasibility of this DCP was investigated by quantifying app engagement, measured by the number of days in the programme participants tracked >1 data point (eg, food intake, bowel movements, digestive complaints and a short list of their most unpredictable or fluctuating symptoms (referred to as 'observations')) and the average number of observations entered on days on which any tracking occurred. Compliance with scheduled weekly virtual coaching sessions was also calculated. The influence of tracking activity and coaching session compliance on HRQoL outcomes was assessed.

DCP intervention

All participants continued their usual care and any changes to their existing medical regimens were directed by outside treating physicians. The DCP is a personalised trial programme that systematises the common and potentially dangerous trial-and-error process attempted by many autoimmune patients to modify their diets, supplements, medications and other environmental and behavioural factors in an effort to improve symptoms. With a data-driven, personalised platform (the mobile app), participants conduct experiments to investigate, isolate and uncover unique associations between complex exposomal variables and symptoms. This is accomplished through participants' digital collection of 'self-evidence' via the mobile app and a proprietary data visualisation tool (the coaching 'dashboard') which allows trained coaches to identify relationships between the timing of exposomal factors and how patients feel. Once exposome–symptom associations are identified, this information is used to guide a joint effort between health coaches and participants to support the participants' decision-making as it relates to food and beverage intake, modifiable environmental exposures (eg, personal care and cleaning products) and other behavioural determinants of health. This process effectively creates a highly personalised and evolving knowledge base and provides patients an important sense of control over seemingly unpredictable symptoms. The interventions recommended include changes to food, beverage and supplement intake, sleep habits, activity level and stress management, as well as to other modifiable exposomal factors which appear to impact symptoms.

The programme consists of three key components: (1) an adaptive mobile app that builds around patients' unique data and allows patients to quickly and easily track select factors in their exposome; (2) a data-presentation dashboard that provides health coaches the tools for data visualisation, analysis and the creation of iterative interventions; and (3) weekly, remote, one-on-one health coaching sessions to review the data correlations, suggest dietary and lifestyle modifications, scrutinise the results of the weeks' previous modifications, and support patients as they implement the changes and add back work and other activities. The app and dashboard serve as user interfaces for the participants and health coaches, respectively. The app also allows participants and their coaches to communicate freely, as needed, through an in-app messaging function.

Participants received initial training on the app functions. All participants were instructed at the start of the DCP to comprehensively track food and drink plus bowel movements on a Bristol Stool Chart.[22] The tracking of food intake was accomplished simply by taking a picture of all consumed foods and beverages on the app. Tracking of symptoms and environmental factors (eg, sleep, physical activity, stress, recreational activities, travel) was personalised and initially based on a 60-minute intake call during which the health coach collected detailed information about an individual's symptoms and behavioural determinants of health. Based on this information, the health coach added fields to a participant's app in order to gather pertinent data (eg, if a participant reported erratic and non-restorative sleep, a field could be created to track bedtime, sleep duration and perceived quality of sleep each night). App customisation included characterising symptom quality and severity in participants' own words to improve tracking accuracy and compliance. The app was regularly updated and adapted by the health coach to reflect each participant's evolution in the programme and to avoid tracking requirements becoming overwhelming.

Health coaches were educated in the conditions treated, trained in the methods of the DCP, and relied on readiness-for-change and active listening techniques to inform their sessions. Coaches monitored and analysed each individual's data in order to: (1) identify potential correlations between diet, medications, supplements, lifestyle and environmental factors and symptoms ('trigger identification'); (2) test those hypotheses by suggesting eating and behaviour modifications; (3) further guide eating and other behavioural interventions based on tracked data; and (4) monitor the results of personalised interventions and make appropriate, iterative adjustments based on symptom response.

In addition to the trigger identification process described, the programme used the following general principles: (1) working towards healthy, daily bowel movements (based on the Bristol Stool Chart); (2) the addition of nutrient-dense foods to the diet if they are deemed lacking (tested against symptoms and potential triggers to ensure any recommended nutritional changes based on standard guidelines did not negatively impact health); (3) individually tailored gentle exercise guidance; (4) ensuring adequate hydration; (5) education and training on good sleep hygiene; (6) mindful breathing and other stress-relieving techniques; and (7)

the use of a limited number of supplements on a case-by-case basis (eg, supplementation with vitamin D if an individual's medical records showed deficiency that was not being repleted) and a review of any existing supplements being taken to identify unhelpful or potentially triggering products (see online supplemental appendix A for full Supplement Use Protocol).

Based on prior experience with the DCP, it was anticipated that EOP would be reached in approximately 16 weeks; however, this varies by individual and ultimately is determined jointly by the participant and health coach and depends on when symptom triggers are identified, successful modifications have been achieved to reduce or eliminate triggers, and participant-defined goals, established at the beginning of the programme, have been met.

Statistical analysis

To account for non-normally distributed data, Wilcoxon matched-pairs tests were used to measure the differences between participants' BL and EOP PROMIS29+MSx scores. These analyses were conducted on the entire population (n=202), subgroups according to primary diagnosis and for those who reported some level of compromise by domain at BL (ie, excluding participants whose BL score was within 1 SD of the reference population score of 50). Regression analyses were used to assess severity at BL as a predictor of reported change in each HRQoL domain (eg, did severity of BL fatigue predict change in any of the 10 PROMIS29+MSx domains). The percentage of participants who met or surpassed MIC was also assessed.

Linear regressions and Kruskal-Wallis H analyses were conducted to assess the influence of descriptive and demographic independent variables on all PROMIS29+MSx outcomes. To account for non-normally distributed data, Kruskal-Wallis H analyses were used to assess group differences in PROMIS29+MSx outcomes between categorical independent variables (sex, employment, marital status, annual household income, education, ethnicity, referral source, coach assignment and paid status). Additional bivariate regression analyses were conducted to assess continuous variables (change in weight, number of weeks in the programme and tracking adherence). If significant associations were revealed, multivariate regression analysis was planned.

RESULTS

Three hundred twenty-five individuals submitted BL data during the study period. Of these, 13 never completed the first coach call. Of the remaining 312 individuals, 202 (64.7%) completed BL and EOP information and were included in the study. For completers, the mean±SD age at BL was 46.2±12.2 years and 77.0% were female. Racial and ethnic distribution were: Caucasian (70.8%), Hispanic/Latino/a (13.9%), Asian (6.4%), African American (3.5%), Native Hawaiian/Pacific Islander (1.5%), Multiracial (1.0%), American Indian/Alaska Native (1.0%) (2.0% preferred not to state) (table 1). Referral sources were as follows: as a covered benefit through health insurance or employer (60%); peer referrals or direct marketing (24%); physician referral (16%). Twelve per cent of participants paid out of pocket for the programme, while the remaining 88% had the fees covered by their health insurer, employer or through promotional programmes. At BL, 75 (37.1%) participants were taking a conventional disease-modifying antirheumatic drug (DMARD); 65 (32.2%), biological DMARD; 15 (7.4%), targeted synthetic DMARD; 9 (4.5%), another immunomodulating drug; 25 (12.4%), oral steroids; 2 (1.0%), topical steroids; and 29 (14.4%) took non-steroidal anti-inflammatory drugs regularly.

Demographic, descriptive and BL PROMIS29+MSx scores of the 110 non-completers are shown in online supplemental appendix B. No differences were found in BL demographic characteristics or BL PROMIS29+MSx domains between completers and non-completers, suggesting no attrition bias.

Diagnoses in completers (table 2) were as follows: RA (20%), long COVID (15%), psoriatic arthritis (11%), psoriasis (9%), SLE (6%), inflammatory bowel disease (6%), multiple sclerosis (6%), ankylosing spondylitis (5%), other AIDs (15%) (online supplemental appendix C) and 9% did not have an autoimmune diagnosis but entered the programme with symptoms and syndromes often seen with AID (for example, chronic fatigue syndrome/myalgic encephalomyelitis, fibromyalgia and irritable bowel syndrome; see online supplemental appendix D for the complete list).

The average time spent in the programme was 17 weeks (range 4–40 weeks). Participants tracked data an average of 86% of the days they were in the programme. The mean number of observations entered per day was 7.6, the mean total observations per participant was 756 and the average number of coaching sessions completed was 14.

Average absolute change in T-score from BL to EOP by domain was as follows: ability to participate in social roles and activities (5.6); cognitive function (3.0); ability to manage symptoms (6.4); physical functioning (3.0); anxiety (−4.2); depression (−3.1); fatigue (−7.8); pain interference (−5.5); sleep disturbance (−5.7); pain intensity (on 0–10 Visual Analogue Scale pain scale) (−1.4). These changes were statistically significant for all domains (table 3).

Results stratified by severity of PROMIS29+MSx score at BL (mild, moderate, severe) were also tabulated. On average, those with the most severe compromise by domain at BL experienced a greater magnitude of change than those beginning the programme with lesser degrees of compromise. When participants who scored within normal limits (ie, within 1 SD of general population mean) at BL were excluded from analyses, the average improvements in the remaining participants exceeded MIC thresholds in every domain (figure 1). For the

Table 1 Demographic and descriptive variables

	N	%	Mean	SD
Age (years)	202		46.2	12.2
17–29	16	8		
30–39	53	26		
40–49	48	24		
50–59	53	26		
60–69	31	15		
70+	1	<1		
Sex, female	156	77		
Race/ethnicity				
White, non-Hispanic/Latino/a	143	71		
White, Hispanic/Latino/a	28	14		
Asian	13	6		
African American	7	3		
Multiracial	3	1		
Native Hawaiian/other Pacific Islander	2	1		
American Indian/Alaska Native	2	1		
Prefer not to state	4	2		
Annual income				
Under $50 000	47	23		
$50 000–$99 999	48	24		
$100 000 or more	54	27		
Prefer not to state	53	26		
Education				
Bachelor's degree	81	40		
Advanced/professional degree	64	32		
Some college, no degree	32	16		
Associates degree	13	6		
High school or equivalent	10	5		
Less than a high school diploma	1	<1		
Prefer not to state	1	<1		
Employment				
Employed full-time	95	47		
Self-employed	33	16		
Employed part-time	21	10		
Unable to work/on disability	17	8		
Unemployed	15	7		
Retired	11	5		
Student	5	2		
Homemaker	4	2		
Prefer not to state	1	<1		
Marital status				
Married or in domestic partnership	116	57		
Single	63	31		
Divorced or separated	14	7		
Widowed	7	3		
Prefer not to state	2	1		

subset of participants who started as either mildly, moderately or severely affected at BL in a particular domain, the percentage who met the MIC threshold (calculated independently for each domain) was determined. For ability to participate in social roles and activities, 58% of participants met the MIC threshold; cognitive function 44%; ability to manage symptoms 57%; physical function 39%; anxiety 50%; depression 39%; fatigue 56%; pain interference 53%; sleep disturbance 59%; pain intensity 41%.

Except for a correlation between sex and change in PROMIS fatigue (see online supplemental appendix E), no other significant relationships were found between sex, marital status, employment, income, education, coach assignment, ethnicity, referral source, paid status, number of weeks in programme, tracking adherence nor change in weight and PROMIS29+MSx outcomes.

Table 2 Distribution of diagnoses*

	N	%
RA	41	20
Long COVID	30	15
PsA	22	11
Psoriasis	18	9
SLE	13	6
MS	12	6
Crohn's/UC	12	6
AS	11	5
Other autoimmune diagnoses†	30	15
No autoimmune diagnosis†	19	9

*Some participants reported more than one diagnosis.
†See online supplemental appendices C and D for lists of other autoimmune diagnoses and description of participants without a definitive autoimmune diagnosis.
AS, ankylosing spondylitis; MS, multiple sclerosis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; UC, ulcerative colitis.

Table 3 Change in PROMIS29+MSx from BL to EOP by domain (n=202)

	Mean at BL	Mean at EOP	Change	P value
Ability to participate in social roles and activities*	46.5	52.1	5.6	<0.0001
Cognitive function*	49.3	52.3	3.0	<0.0001
Ability to manage symptoms*	43.3	49.7	6.4	<0.0001
Physical function*	44.4	47.4	3.0	<0.0001
Anxiety†	55.7	51.5	−4.2	<0.0001
Depression†	51.3	48.2	−3.1	<0.0001
Fatigue†	58.3	50.5	−7.8	<0.0001
Pain interference†	56.9	51.5	−5.5	<0.0001
Sleep disturbance†	53.4	47.7	−5.7	<0.0001
Pain intensity†‡	4.0	2.5	−1.4	<0.0001

*Higher score indicates improvement.
†Lower score indicates improvement.
‡Pain intensity was measured on a 0–10 VAS.
BL, baseline; EOP, end of programme; VAS, Visual Analogue Scale.

Changes from BL to EOP in PROMIS29+MSx scores were analysed when participants were stratified by diagnosis. Trends toward improvement were seen in every domain in each diagnosis group and remained statistically significant in many (table 4).

This study did include 19 participants who did not carry a definitive autoimmune diagnosis but had manifestations of or syndromes often coincident with AID. Analyses were run excluding these 19 individuals and results were not substantively changed—change in PROMIS29+MSx scores from BL to EOP in the remaining 183 individuals remained statistically significant with p<0.0001 in each domain (see online supplemental appendix F).

When tracking logs were interrogated, over 100 unique triggers (including dozens of food triggers) were related to over 50 symptoms. The most prevalent trigger categories were: excessive or insufficient intake of foods, specific food ingredients, nutrients or beverages; non-restorative sleep; psychosocial stress; and suboptimal levels of movement or exercise. While overconsumption of a range of frequently suspected foods, such as refined carbohydrates, carbohydrate constituents, processed meats and stimulants, were identified, almost equal numbers of healthful foods, supplements and medications were found to be problematic for some participants. Examples include tomatoes, almonds, carrots, bananas, avocados and apples, and immune-modulating and anti-inflammatory medications, even in small quantities. Direct, one-to-one correlations between a single trigger and one or more symptoms existed; however, several complex patterns also emerged. Combinations of triggers were identified to have a compounding effect on one another. Some participants' symptoms followed triggers after each exposure, whereas in others, symptoms followed specific triggers only at certain threshold levels (eg, consumption >2×/day), when the participant had not been sleeping well, or seasonally (eg, only when consumed in certain seasons). Many participants required a combination of interventions (eg, trigger reduction or removal, nutrient-dense food additions and sleep or activity modification) to achieve meaningful symptom improvement.

DISCUSSION

This study demonstrates that a highly personalised, data-driven DCP has the potential to meaningfully improve HRQoL in individuals with a variety of AIDs, AID-related conditions and long COVID. Statistically significant improvements, exceeding MIC thresholds, were seen in multiple PROMIS29+MSx domains and were independent of several potentially confounding variables. Severity of compromise at BL and magnitude of improvement were directly correlated across multiple domains.

This study builds on a growing body of research examining the relationship between diet, lifestyle, and health behaviours and AIDs. Tedeschi *et al* surveyed 300 patients with RA and found that close to one-quarter reported that diet had an effect on their RA symptoms.[23] Similarly, 28% of 704 surveyed patients with RA reported either favourable or unfavourable effects of specific foods on clinical status. Interestingly, in several cases, the same food group (eg, citrus, fish, dairy) was reported by some respondents as having a favourable effect, while in others the effect was unfavourable.[24] As compared with the rapidly expanding knowledge base on diet and AID, a much smaller but still compelling body of research is emerging focused on the influence of sleep,[11 12 24–26] physical activity[13 14 27 28] and stress[15 16 29 30] on immune-mediated conditions. The results suggest that these modifiable lifestyle factors play an important role in the development and progression of AID but with effects that are complex and heterogeneous.

The strengths of this investigation include its real-world setting, demonstrating acceptability and feasibility of the DCP outside of a study environment. Sixty-five per

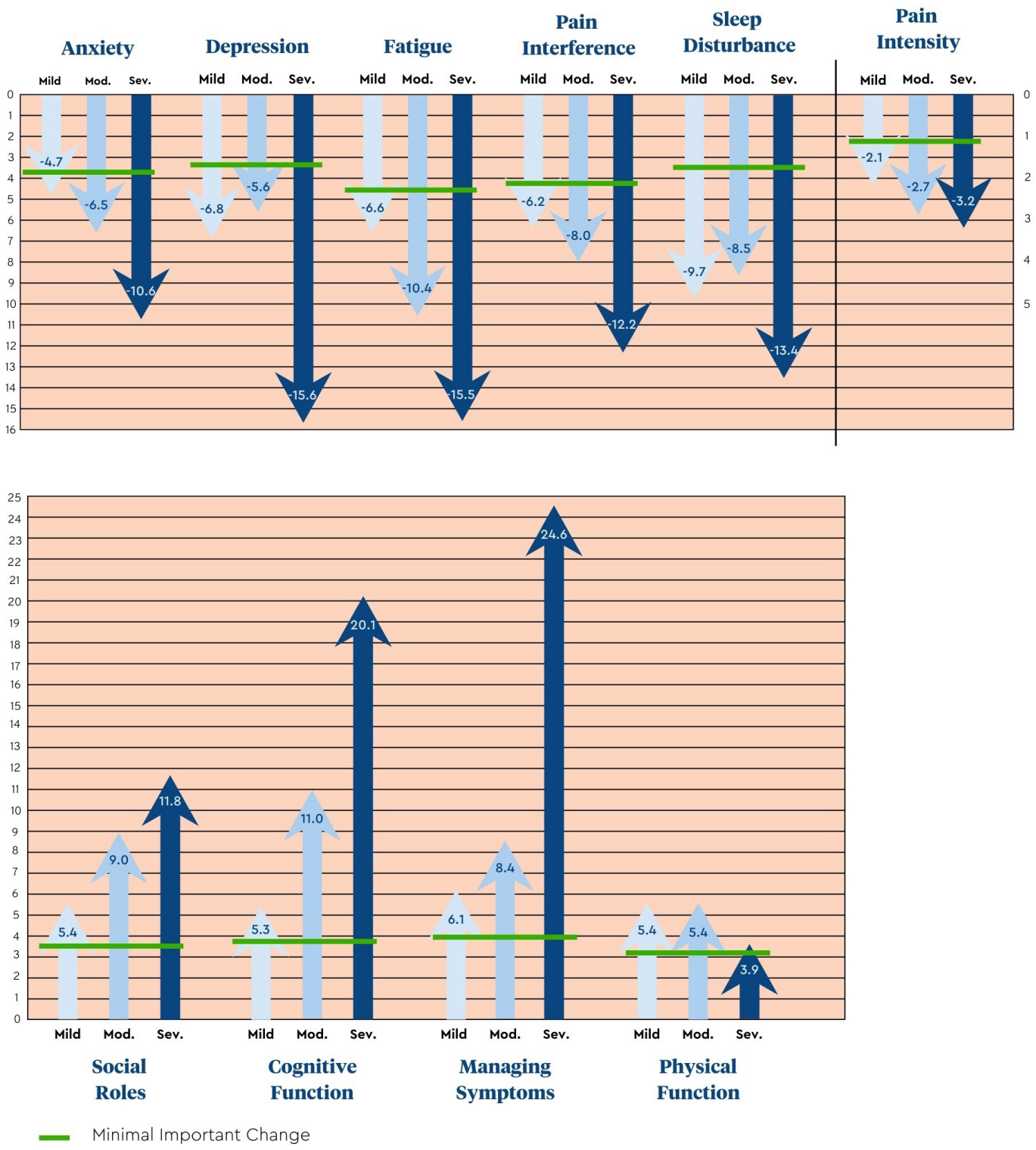

Figure 1 (A) Change in PROMIS from baseline (BL) to end of programme (EOP) by severity at BL (lower score=improvement). (B) Change in PROMIS29+MSx from BL to EOP by severity at BL (higher score=improvement). PROMIS, Patient-Reported Outcomes Measurement Information System.

cent of participants who engaged in at least one regular coaching session went on to complete the programme. Participants came from diverse ethnic, socioeconomic and educational backgrounds and had a variety of autoimmune diagnoses, supporting its wide applicability. PROMIS is a robust and validated system for measuring HRQoL and is sensitive to detecting change over time.[31] In RA, PROMIS has been shown to correlate with the Clinical Disease Activity Index, therefore may prove valuable as a proxy for clinical disease activity measures.[32] What constitutes a clinically meaningful change in PROMIS scores in patients with AID has been the topic of several

Table 4 Mean change in PROMIS29+MSx (±SD) by diagnosis

Domain (MIC)	RA (n=41)	LC (n=30)	PsA (n=22)	PsO (n=18)	SLE (n=13)	IBD (n=12)	MS (n=12)	AS (n=11)	Other AIDs (n=30)	No AID (n=19)
Soc roles (3.7)	**6.9** (7.9)	**5.1** (7.1)	**6.1** (6.9)	**5.0** (7.0)	**6.6** (7.5)	*1.7* *(4.7)*	*1.8* *(4.9)*	**9.9** (4.8)	**6.7** (8.3)	*3.3* *(7.5)*
Cog func (3.9)	**2.8** (5.8)	**4.4** (7.1)	*2.0* *(5.6)*	**4.1** (7.4)	**5.7** (6.2)	*–0.8* *(8.6)*	**5.8** (9.6)	*4.5* *(7.6)*	**2.2** (8.5)	*1.5* *(10.5)*
Man sx (4.0)	**8.7** (9.0)	**6.7** (6.6)	**5.1** (7.3)	*4.3* *(8.5)*	*3.3* *(8.2)*	**7.0** (9.1)	**8.0** (6.1)	*5.2* *(7.8)*	**5.6** (7.1)	**7.2** (7.9)
Phys func (3.2)	**3.3** (6.4)	**5.6** (5.1)	**4.0** (7.1)	*1.0* *(6.3)*	*3.5* *(7.7)*	**3.5** (4.7)	*–0.9* *(5.2)*	*2.6* *(5.9)*	**4.1** (7.7)	*0.5* *(5.2)*
Anx (–3.7)	**–4.1** (6.7)	**–5.6** (7.3)	**–4.9** (7.3)	*–3.7* *(7.3)*	**–4.8** (7.6)	*–1.6* *(5.7)*	*–0.7* *(7.3)*	*–6.6* *(8.7)*	**–4.8** (7.4)	**–5.1** (8.2)
Depres (–3.3)	**–3.5** (6.3)	**–4.7** (6.1)	*–2.1* *(6.8)*	*–1.6* *(6.8)*	*–4.1* *(7.9)*	*–2.8* *(6.0)*	*–3.1* *(7.3)*	**–4.9** (5.7)	*–2.1* *(7.1)*	**–4.2** (5.8)
Fatigue (–4.9)	**–7.8** (11.1)	**–9.0** (9.4)	**–8.2** (11.7)	**–7.1** (10.9)	**–11.8** (7.1)	*–3.2* *(8.3)*	**–6.9** (5.8)	**–7.3** (7.7)	**–7.8** (9.7)	**–10.1** (9.2)
P interf (–4.2)	**–7.1** (9.1)	**–5.1** (10.0)	**–6.6** (7.9)	**–4.6** (9.5)	**–4.1** (6.1)	**–5.6** (6.3)	*–3.6* *(9.4)*	**–5.7** (3.7)	**–6.4** (7.8)	**–4.9** (8.3)
Sleep (–3.8)	**–7.0** (6.8)	**–6.0** (7.0)	**–6.4** (8.7)	**–7.1** (8.4)	**–6.8** (8.2)	*–2.0* *(7.8)*	**–6.8** (4.0)	**–6.6** (7.9)	**–3.9** (8.1)	**–5.0** (6.0)
P intens (–1.1)	**–1.9** (2.3)	*–1.0* *(2.6)*	**–2.1** (2.5)	*–1.0* *(2.1)*	**–2.5** (2.3)	**–1.8** (1.5)	*–1.4* *(2.1)*	*–0.8* *(2.0)*	**–1.0** (1.8)	**–1.4** (1.8)

Values in black bold text were statistically significant; values in italicised text were not statistically significant.
MIC was established by domain using descriptive statistics (mean and SD in T-scores) to define thresholds 0.5 SDs from the mean.
AID, autoimmune disease; Anx, anxiety; AS, ankylosing spondylitis; Depres, depression; Cog func, cognitive function; IBD, inflammatory bowel disease; LC, long COVID; Man sx, ability to manage symptoms; MIC, minimal important change; MS, multiple sclerosis; Phys func, physical function; P intens, pain intensity; P interf, pain interference; PsA, psoriatic arthritis; PsO, psoriasis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; Sleep, sleep disturbance; Soc roles, ability to participate in social roles and activities.

investigations. Changes between 2 and 7 points are typically considered to represent meaningful improvement.[31 33 34] The average changes reported by all-comers in this study generally fall within the above parameters. When only those participants who scored outside 1 SD of the population mean in a particular domain at BL (ie, those who were compromised at programme start by domain) were analysed, the magnitudes of change were greater and often exceeded MIC thresholds. The degrees of change seen in this study can also be compared with those reported by a population with active RA 12 weeks after initiating DMARD treatment. Improvements in that study group ranged from 2.0 to 6.0 points in the domains of anxiety, depression, fatigue, pain interference, sleep disturbance and pain intensity.[35] Comparable scores from all-comers and only those with RA in this study population were 3.1–7.7 and 1.9–7.8, respectively; when considering only the participants who scored below the general population average at BL in this study, the changes ranged from 6.0 to 10.3.

This study has several limitations. As this was retrospective, participants were not randomised or blinded and there was no control group; therefore, the results are subject to selection and performance biases and exaggeration of effect size. Comparison of the available BL demographic and HRQoL data revealed no statistically significant differences between completers and non-completers; however, it is not clear if analysis of other variables would reveal systematic differences between these groups to account for attrition. As PROMIS29+MSx data were only available for individuals who completed the programme, the generalisability and external validity of the results are limited by this non-response sampling bias and must be interpreted with caution. By design, the DCP is a multidimensional intervention; without a control group, this study cannot provide insight into whether individual facets of the programme (ie, different aspects of patient digital engagement, the data-informed interventions, interaction with health coaches) contributed more or less to the achieved results or if, in fact, it is the integration of these facets that accounts for the observed outcomes. Although diverse ethnic backgrounds were represented, African American individuals were underrepresented as a percentage of the population as a whole and with respect to their prevalence of AID.[36] Participant diagnoses were largely self-reported; therefore, whether formal diagnostic criteria were met for each diagnosis was not ascertained. However, participant-provided medication lists and medical histories were considered to be consistent with the patient-designated diagnoses.

The positive results of the experimental intervention on HRQoL in those completing the programme raise

numerous important questions regarding the underlying mechanism of action of the intervention. Given that the study was not designed to investigate putative mechanisms of action, this will be an important focus in future work to understand how these individualised dietary and lifestyle changes impact patient biology. Potential effects of the intervention include diet-influenced changes to the gut microbiome and metabolome which, in turn, may influence epigenetic phenomena critical to the development and ongoing activity of AID.[7 37–40] In addition, the role of dietary triggers of autoimmunity at the individual level is complex and, given that it was incompletely investigated here, will require more systematic assessments in future studies. Finally, as the current study is unblinded, important questions are raised regarding the role of placebo effects in influencing HRQoL. This is important to consider, for in clinical settings, it is well documented that expectancies can be affected by the way in which a medication or treatment is described or 'framed' which, in turn, can potentially influence numerous variables related to HRQoL, including pain.[41] Future studies should include a control group of an acceptable design to allow for examination of the influence of the nature of messaging provided by the health coach and the patient's susceptibility to placebo effects, which can be assessed through pre-intervention profiling.[41]

The groundbreaking work being done to unravel the complex interplay between diet, lifestyle, environmental factors, the gut microbiome and epigenetics with AID parallels an increasing interest from patients in complementary self-management strategies to improve symptom control and decrease reliance on medication. Over a 12-month period in the USA alone, $33.9 billion was spent out of pocket on complementary medicine.[42] It is estimated that greater than 50% of patients with SLE have tried at least one complementary medicine modality.[43] In a survey of 300 patients with SLE, 100% of respondents said that they would alter their diet if it would improve their condition, particularly with respect to fatigue and managing disease flares, and 83% would enrol in diet-based clinical trials if available.[44] A survey of 420 patients with lupus in the UK provided provocative data attesting to the interest in and self-driven action taken on dietary modifications in this population. Sixty-one per cent reported deliberately eating or avoiding certain foods to 'control my lupus symptoms', while 57% avoided certain foods because 'they make my lupus symptoms worse'. For those who had not changed eating habits, the reasons were not having enough information (41%), worrying it would make lupus symptoms worse (31%) and lack of willpower (25%). The range of dietary changes was broad—20 distinct dietary patterns were reported by respondents (plus 10% who indicated 'other dietary patterns'). Finally, all but one respondent reported that they would entertain changes to their eating habits if told it would improve symptoms.[45]

This interest should be leveraged and reinforced by a continually evolving, self-evidence-based understanding of how food, lifestyle and environmental exposures influence disease. Without full participation and dedication of medical and research communities to this undertaking, patients will be left experimenting on their own with diet and behaviour modifications at the risk of putting effort and money into solutions that may not help (creating frustration and resignation) or, worse yet, those that can cause harm. There is a glut of advice on the internet, with widely variable degrees of supportive evidence, for people with AID looking to enhance their treatment with special diets, dietary supplements and other alternative solutions. Multiple books claim to have the answer for the best way to eat for patients with AID; some endorse a ketogenic diet, others palaeolithic or Mediterranean diets—and many patients have found different degrees of relief following these protocols. However, these one-size-fits-all solutions fail to take into account the great variability in individual immune responses and sensitivities and are not without risks, especially if done unsupervised. It is imperative that patient interest in dietary guidance and complementary medicine is met with respect, genuine consideration and rigorous study by experts in the field so that the full benefits of these modalities can be realised and risks and exploitation minimised. Incorporating personalised, non-pharmocological care recommendations—low-risk and relatively inexpensive interventions—into the standard of care for AIDs also has tremendous potential for direct and indirect cost-savings in an area of medicine with increasing prevalence and high per-patient expenditures.

In summary, this work demonstrates that a DCP is feasible and acceptable to a wide variety of individuals with AIDs, AID-related syndromes and long COVID. The personalised interventions generated by the programme were associated with statistically significant, clinically meaningful improvements in multiple domains germane to HRQoL as measured by PROMIS29+MSx. The findings add to a growing body of research that supports the inclusion of diet and lifestyle interventions in the management of AIDs. The results should act as a catalyst for increased funding and further exploration into the application of personalised trials to optimise the success of such interventions in individual patients.

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Competing interests NB is a paid consultant for Mymee and has ownership in the company. MDJ is paid as an independent contractor by Mymee. ML is a salaried employee of Mymee. LC serves on the Board of Scientific Advisors for Mymee. MD is employed by Mymee and has ownership in the company. There are no other competing interests to disclose. NB is the guarator for this paper.

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