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A hand exercise mobile app for people with rheumatoid arthritis in Turkey: design, development and usability study

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Abstract

To design and develop a smartphone application for a structured hand exercise programme for patients with rheumatoid arthritis (RA) in Turkey and to test its usability. We followed a two-stage process: (1) Design and Development and (2) Usability testing. In stage 1, we used a qualitative user-centered design approach. We conducted a focus group (8 therapists and people with RA) to discuss the content, features and design to produce a prototype of the application. In a second focus group session, the participants tested the prototype, provided feedback and further revisions were made. In stage 2, 17 participants with RA used the app for 4 to 6 weeks. The System Usability Scale and the adapted Usability, Satisfaction and Ease to Use Questionnaires were used to measure usability, ease of use. Semi-structured interviews were conducted to explore user experiences with the application with 17 participants. In stage 1, the following themes were identified from the focus groups (a) login techniques (b) self-monitoring (c) exercises, (d) exercise diary, (e) information, (f) behavioral change and encouragement (g) exercise adherence. In stage 2, 3 themes were determined from interviews: (a) learning and accuracy, (b) ease of use, (c) motivation and adherence. USE and SUS scores indicated that users reported a high level of usability, satisfaction and ease of use. A mobile app for hand exercise for people with RA was developed using a mixed-method and iterative design. Participants perceived the mobile app as easy to use with high levels of satisfaction.

Keywords Mobile applications · Exercise · Hand · Rheumatoid arthritis · MHealth · Qualitative research

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease that can affect a multiple synovial joint, especially the small joints of the hands and wrists [1, 2]. Hand function is considerably reduced due to pain, decreased grip strength, reduced joint range of motion and deformities [3, 4]. According to international clinical guidelines, structured hand exercise programmes are recommended for patients with RA affecting their hands [5]. One such programme is the Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH) program which has been shown to provide long term improvement in hand function for patients with RA [6]. The SARAH programme is delivered over 5 sessions with a hand therapist and the patient is asked to carry out exercises at home on a daily basis. To support the home exercises, to reduce the number of hand therapy sessions required and to make it easier for patients to access the SARAH programme, a web-based version of the programme (mySARAH) was developed for patients in english. Preliminary evaluation has found this is an acceptive and effective way to deliver the SARAH programme [7].

Digital health is the integration of digital technologies with health, life and society to increase the effectiveness of healthcare delivery and to provide personalised care [8]. Digital rehabilitation provides a rehabilitation service remotely via digital/telecommunication technology. It is a way to provide easy access to rehabilitation services for those that need

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them regularly with reduced burden of travel to appointments resulting in time, labour force and cost savings [10, 11]. Digital rehabilitation interventions have the potential to support patients by providing clinicians with a means of encouraging self-management and motivating patients to undertake home exercises [12, 13].

The widespread use of mobile devices, such as cell phones and tablets, has led to the creation of mobile health (mHealth) products to deliver digital health interventions. mhealth describes medical and public health interventions supported by mobile devices, such as cell phones and tablets. The popularity, portability, and technological features of mobile technology provide an advantageous basis for improving healthcare delivery processes [8, 9]. Mobile health apps technology can provide an easy, usable, and accessible platform for utilizing rehabilitation interventions. In the field of mobile applications, a new developing market has emerged that supports the rehabilitation of patients, especially regarding the adherence to home exercises [14, 15]. These systems focus on engagement with exercise interventions through personalized goal setting, exercise reminders, and motivational message notifications. In addition, the advanced monitoring, data collection and real-time notification features of mhealth apps are advantageous to both researchers and healthcare professionals [16]. Increasingly, research evidence supports the effectiveness of mHealth interventions for improved exercise adherence and motivation [17–19].

Numerous mHealth applications exist to support users in the self-management of the musculoskeletal disorders and arthritis [13, 17–19]. But most of these apps were not designed with input from both users and health professionals [20]. In a study which explored the benefits of smartphone applications for patients with RA and their perspectives about rehabilitation applications, 94% participants stated that these programmes have a crucial role for self-care, 86% were willing to use it, and 86% would like to buy these programmes [21].

In Turkey, the number of physiotherapists who work in rheumatology departments is considerably low. Therefore, there is an opportunity to use the mHealth app technologies for exercise prescription and patient monitoring. Majority of the Turkish population have access to a smartphone and internet services. A mobile app was therefore considered to deliver the hand exercises to people with RA in Turkey.

The aim was to develop a mHealth app using an iterative user-centred design approach to ensure the product met user needs, was easy to use and acceptable to both patients with RA and therapists [22, 23] and test its usability.

Methods

We followed a two-stage process: (a) Design and Development b) Usability (see Fig. 1). During the design and development stage, we produced the prototype and then revised it following feedback from a focus group (therapists and patients) before undertaking usability testing.

The study protocol was approved by the Clinical Research Ethics Committee of Marmara University Medical Faculty. All participants provided informed consent prior to participation.

Participants

(a) Design and development stage: therapists (physiotherapists or hand therapists) with at least 5 years working experience in the field of rheumatology or hand therapy departments, and patients who had previously received hand therapy with the diagnosis of RA were invited to the focus groups. Focus group members took part in phase I and II. Quota sampling method was used to recruit focus group participants via personal network of researchers [24]. Participants were invited by email or phone call. The participants completed a brief demographic questionnaire before the first focus group session.

(b) Usability: participants were recruited from Haydarpasa Numune Research and Education Hospital, Rheumatology Clinic. We aimed to recruit 20 volunteers with a diagnosis of RA who have hand involvement. Based on the existing evidence, 95% of usability problems can be identified with 20 users [25, 26]. Patients did not receive any other physiotherapy intervention or injections during the study period.

Design and development

This stage consisted of two phases:

Phase 1-development of hand exercise smartphone software for patients with RA (prototype version software/ MarHand therapy app)

Focus groups were held to discuss the content, feature and design of the app. This information informed the production of the app prototype. Discussions were led by the lead author who presented an overview of hand therapy programs available in published literature and in clinical guidelines for patients with RA. An introduction to the SARAH hand exercises for adults with RA, as recommended in the guidelines, was provided. A series of open-ended questions (See Supplementary file 1) were asked and participants discussed

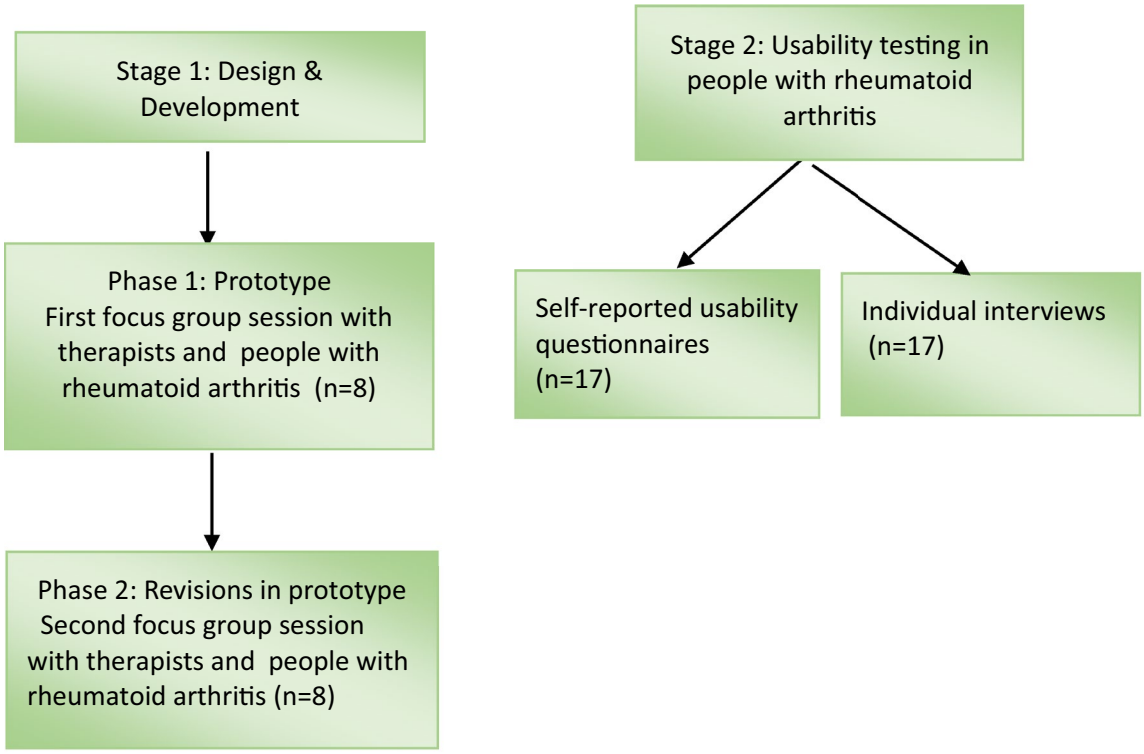

Fig. 1 Study flowchart

a variety of topics including advantages/disadvantages of a mobile app, login parameters, self-monitoring, exercise content, video or animation types, exercise diary, reminders, ways to encourage and motivate the user to exercise and the type of advice to be included. The focus group sessions were audio-recorded and transcribed verbatim.

Phase 2-testing the app prototype (revised-MarHand therapy app)

Focus group members were asked to use the app for 1 week. They were asked to provide written feedback regarding the technical errors and faults encountered while using the different elements of the app including login, evaluation and questionnaires, videos, notifications and reminders. A second focus group (See question guide in Supplementary file 1) was held to discuss their experiences and possible modifications.

Usability testing

Participants attended an app demonstration session with the lead author in groups of five. The different elements of the application were demonstrated, and their use was explained. Each session took around 20 min. Participants were asked to open the app, follow the instructions and complete the exercise prescription form (choosing exercises and reminders, number of times/day and time of day). They were asked to use the app on their own for 4 to 6 weeks. During the 7th week, we conducted the usability tests and interviews.

Usability was tested in two ways:

(a) Quantitative data

Cloud MangoDB Atlas software, a user activation tracking system, was used to track interaction of participants with exercise videos measuring daily/weekly/total time (seconds) of interactions and number of interactions.

Users completed the System Usability Scale (SUS) [27, 28] which ranges from 0 to 100, with higher scores representing greater usability. For each participant, the mean SUS scores (0–100) were calculated and transformed into a usability score out of 100.

User also completed the adapted Usability, Satisfaction and Ease to Use (USE) Questionnaire [29, 30]. We adapted the USE questionnaire to assess usability specific to our application. The adapted questionnaire had 10 questions and each question was scored on a Likert scale (1/5) (supplementary file 1) with two domains (Ease of use and Satisfaction). The mean score for each domain of the USE questionnaire was calculated for each participant. The higher scores indicated greater usability for USE.

(b)Qualitative data

Individual semi-structured face-to-face interviews were conducted 6 weeks after introducing participants to the app. We used open-ended questions following an interview guide (Supplementary file 1). The interviews were audio-recorded and transcribed verbatim.

Analysis

The Qualitative Research Data Analysis Software QSR NVivo 11 was used to organize the qualitative data from the focus groups and interviews [31]. Thematic analysis was performed as described by Braun and Clarke [32]. Throughout the process, the research team met to discuss the data and alternative interpretations of the data. Data were assigned with codes, and codes with similar content were grouped into thematic categories. Quantitative data are presented descriptively. Categorical data are summarized as numbers of participants in each category. Continuous data are summarized as the mean (standard deviation) or median (interquartile range). We used Statistical Package for the Social Sciences software (SPSS, IBM, version 20.0; Armonk, NY, USA).

Results

Stage 1: design and development

Majority of the therapists were female (4/5), with age range between 30 and 40 years. All three patients in the focus group were women (age of patients (years): 36, 45, 65).

Phase 1 (prototyping)

Seven themes relating to user needs and requirements for the mobile app were identified from the focus group interviews. Participant quotes supporting each theme as well as solutions to address the identified needs and requirements are presented in Table 1.

- **Theme 1** Logging into app

  Patients and therapists all agreed that the login methods must be easy to use. In response to this, we added a tab to the app that contains instructions on how to use the app with a notification to access this following the login stage. In addition, we recommended a brief (face to face or online, individual or group) training session be provided by therapists for patients who will use this app. When patients access the instruction tab, there is a recommendation that they see their therapist for a short training session if they have not done so already.

- **Theme 2** Self-monitoring

  Patients wanted to track their pain intensity and hand function. All therapists remarked that hand pain, hand function and satisfaction levels are important assessments. They added the questionnaires used in the app should not be too long to ensure they were fully completed. So, it was agreed to use two short hand function questionnaires. The selected self-monitoring assessments are on Table 1. They also added that it would be helpful if the therapist could see the results of patient outcomes in a graph. To address this, the app was connected to Cloud MangoDB Atlas software that allows data to be exported into Microsoft word, Excel programs and visualization by graphs or tables.

- **Theme 3** Exercises

  The therapists felt that the SARAH exercises were beneficial for their patients and felt they were appropriate to include in the app. For patients, not including too many exercises was important and some specific types of exercises (the SARAH exercises and additional tendon gliding exercises) they had previously benefited from were mentioned. Patients recommended a maximum of eight exercises be prescribed at one time, as more exercises may make people reluctant to do them regularly. Consequently, seven hand exercises were chosen from the eleven SARAH programme exercises with a few adaptations (see Table 1). All focus group members recommended including exercise demonstration videos with clear instructions.

- **Theme 4** Exercise diary

  Therapists recommended that patient should do the exercises 3 days a week (5–8 repetitions), they also suggested that patients should choose the days and time when they would do the exercises. To accommodate this, we designed the exercise diary allowing patients to choose their schedule (days of the week, and the time) for doing the exercises. The software sends notifications to remind the user to do their exercises 1 h before the selected time. There are four reminders.

- **Theme 5** Information

  All therapists discussed the possible content related to patient education. All of them agreed that the focus was on exercise rather than patient education. One patient suggested that patient education in RA in the form of podcast would be helpful. We added a tab for a podcast which is currently not active but could be developed in the future.

- **Theme 6** Behavior change and encouragement

  Patients wanted exercise reminders and push-up notifications for encouragement, and to be able to chat with an expert if needed. We recommend to HPs who plan to use the app with their patients offer support phone calls when required. Three of the five therapists suggested the

Table 1 Design and Development stage (Prototype version software): solutions for determined themes with sample quotes

Themes	Sample quotes	Solutions
(1) Logging into app	HP: 'login method should be easy. It is very important to guide the patients, if it is possible someone should help patients log-in P: 'I don't know how to download the apps, my granddaughter helped me to organize my smartphone, I'm using WhatsApp and Instagram well now, but someone should login for me and teach me how to use it'	An easy registration system with email address and password creation was followed A tab that contains instructions on how to use the app One brief face to face or online/individual or group training session were recommended to HPs at the instructions tab
(2) Self-monitoring	HP: 'hand pain, hand function and satisfaction levels are important. MHQ and MAP-Hand are for patients with RA' P: 'it would be nice if I can see my own hand status in a separate part so that I can see my improvement'	Hand pain levels (0–10 scale)/Hand fatigue levels (0–10 scale) Hand function: Likert scale, MHQ, MAP-Hand Exporting of outcomes is possible with tracking system
(3) Exercises	HP: 'We already use the SARAH exercises for hour home program successfully' P: 'it is ok for doing 5 to 8 exercises, but if there are too many exercises on the list, I will possibly get bored'	We chose six SARAH exercises: MCP flexion, tendon gliding, radial finger walking, gross grip, finger pinch, wrist extension We made a few modifications to SARAH: (a) unlike the SARAH protocol, elastic band was not preferred for wrist extension. (b) we added a wrist flexion exercise Exercise demonstration videos were recorded
(4) Exercise diary	HP: '3 days a week, 5–8 repetition is suitable in my opinion' HP: 'it is better if patient choose the days of exercise in the diary'	Patients choose the schedule (days per week, times per day) for doing exercise
(5) Information	HP: 'the aim of the app is mainly about exercise, if the patient wanted to have information about diseases there are lots of websites' P: 'it will be nice to listen to some short information like in a podcast'	We have no tab about disease specific information. But we added an optional section for adding the podcasts in future
(6) Behavior change and encouragement	P: 'morning and after work push up messages will be nice'. One patient said, "it will be nice to chat once a week with my therapist in order to progress through the, maybe a video call" HP: 'patients want motivational messages, lets write some messages for morning, afternoon and evening messages, and decide how many messages to use'	Recommendation about weekly follow up contact with patients were given at instructions tab Motivational short messages about exercises. (total ten messages which were sent randomly two times a day) Examples: "Good morning lets be more active today", "break time at work, would you like to do some tendon gliding exercise", "let's move our hand joints"
(7) Exercise adherence	HP: 'It would be useful if we can see the patient's activation on phone P:'someone should check with me to see whether I'm ok with my app'	Codes were written for app's software to track user activity. So, HP's can follow up the interaction with app

HP health professional, *P* participant, *MCP* metacarpophalangeal, *MHQ* brief Michigan Hand Outcomes Questionnaire, *MAP*-hand measure of activity performance of hand (18 item)

addition of push-up notifications as a way to encourage patients to exercise. Short motivational messages about doing regular exercise have been prepared and included as push notifications (see Table 3).

- **Theme 7** Exercise adherence

  Therapists agreed that the app would help patients adhere to their home exercises. They agreed it would be helpful to monitor the adherence using a user activation tracking system. They indicated that in this way, they could follow their patients' engagement with the programme. Based on this discussion, new features were created including a tracking system to assess the frequency and duration of usage of the app (see Table 3).

Initial build of the app

The resulting app had the following sections.

Instructions

Brief instructions on how to use the app.

Outcome measures

Hand pain, hand fatigue, hand function (see Table 1).

Exercise diary

Patients are asked to choose the days and times on which they plan to do their exercises.

Exercises

Seven hand exercises were chosen from the SARAH programme exercises with a few adaptations (see Table 1).

The prototype application was built in June 2019. It is a native app that can be used on both Google Android and Apple IOS operating systems.

Phase 2

The participants who tested the app interface owned different brands of smartphones. Focus group members and volunteer users found some problems and errors. The font size of the text was too small. Users also received error messages. Notifications came up at the wrong time. An option tab to allow the user to play the videos one by one or at all at once was suggested.

Based on therapist feedback, patients had to complete the exercise diary to move onto the next exercise. A Therapist said "In my opinion, filling the exercise diary should be obligatory for using the app, otherwise patients don't care about it and we may not see the data". Visual and sound effects of push-up notifications were changed as recommended by the patients.

Changes to the app in response to feedback

Technical errors identified during phase 2 were fixed by software developers. We added a tab for the exercise videos with two options to the app as follows: 'start selected exercise', 'start all exercises one after the other'. Visual and sound effects were upgraded. Screenshots from app is in Fig. 2.

Stage 2: usability

Twenty participants were recruited for the usability testing. Three participants withdrew due to lack of time. Seventeen participants (males/females: 1/16) used the app. The duration of RA varied among participants ranging from some diagnosed recently to those with longstanding RA. Ten of the 17 patients had previously received a home exercise program. Nearly 40% of the participants had high school level of education, and 65% were not working (Table 2).

Usage status of the app was determined by activation tracking system. Participants were asked to use the app over 6-week period. Total usage status (count of interaction to app, count of participated sessions, usage times) for every individual and average usage (median/IQR) were reported in Table 3. Three participants used the app for the full 6 weeks. Some of the participants ($n=7$) completed more than 9 sessions over 4 weeks, while some of them had very low usage with under 3 sessions ($n=4$). The median number of sessions was 7 (IQR 2.5–12), the median number of uses per/week was 3.5 (IQR 1.5–3), the median total

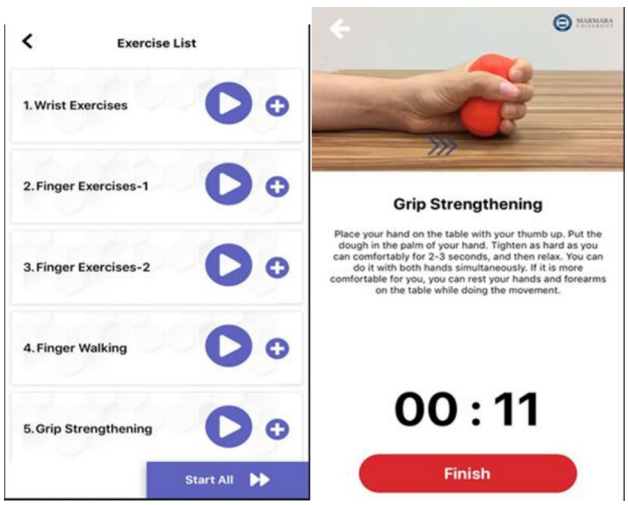

Fig. 2 Screenshots from app

Table 2 Stage 2 Usability testing: demographic characteristics of participants ($n = 17$)

	Median or *n*	Interquartile range (IQR) or *n*%
Gender		
Male	1	6
Female	16	94
Age (year)	48	39–61
Height (cm)	160	158–164
Weight (Kg)	72	57–82
Disease duration	*n*	%
6 months–1 year	3	18
1–2 year	5	29
3–5 year	4	23
5–10 year	2	12
Over 10 year	3	18
Education level	*n*	%
Primary school	5	29
Secondary school	3	18
High school	7	41
University degree	2	12
Working status	*n*	%
Full time worker	3	18
Does not work (or unemployed)	11	64
Retired	3	18

number of interactions with the exercise section of the app was 45 (IQR 22.5–89) and the median total usage time was 70 minute (IQR 19-216).

We reported weekly usage changes over time in Table 4. The number of sessions and usage time of participants decreased over the 6-week period. During the first week, 17 participants used the app with only three still using during the 6th week.

Quantitative and qualitative usability test results at below.

Quantitative data: the median score of the SUS was 100 (IQR 100–100) representing good usability [22]. Participants agreed that the application was easy to use (USE/median easy to use score: 5.00, IQR 4.55–5.00) and would recommend the app to others. All participants agreed that the app was useful and satisfactory (USE/median satisfaction score: 4.88, IQR 4.95–5.0).

Qualitative data: during the face-to-face interviews, participants' experience with the app during the 4–6-week period was discussed. All the participants reported that the app was very useful for hand rehabilitation. Three themes were identified from the narratives.

a) Learning and accuracy

Ten out of 17 participants perceived that the app was useful when it comes to learning the exercises and ensuring they were done correctly. Five individuals stated that after 2 weeks of using the app, they were able to perform the exercises without looking at the videos and only watched them if they forgot the movement or starting position. They

Table 3 App usage status

Participant number	Total number of sessions	Number of weeks using the app	Number of interactions with the exercises	Total usage time (minute)
1	3	1	34	27
2	12	5	131	335
3	11	4	68	349
4	1	1	7	11
5	6	3	45	8
6	5	5	36	54
7	7	3	53	61
8	13	5	84	204
9	3	3	24	461
10	1	1	3	3
11	14	6	101	173
12	8	2	52	150
13	11	4	41	51
14	14	6	94	229
15	2	2	21	70
16	2	2	7	10
17	12	5	116	151

Table 4 Weekly usage changes of app

Weeks	Users (*n*)	Number of sessions		Total usage time (minute)	
		Median	IQR*	Median	IQR*
1 week	17	3	2–4.5	36	15–83
2 week	10	3	2–3	39	18–69
3 week	11	2	1–3	14	0.85–29
4 week	7	1	1–2	20	9–60
5 week	6	1.5	1–3	18	9–60
6 week	3	1	–	19	–

*Interquartile range

felt that the videos helped them to do the exercises correctly with instructions that were easily understood.

One participant said 'videos were so clear that I could distinguish the speed of movement and the direction of joint movement very well. Movement direction animations on the videos were also very convenient when making motion.'

Eight participants compared the benefits of using the app to traditional exercise leaflet and felt the application was very useful in learning the exercises. One participant said, "I received a physiotherapy home programme many times. I understood after my therapist showed me the exercises but then I forgot it. It was not possible to learn the exercise from the brochure, the app allowed me to both learn the exercises and do them safely."

b) Ease of use

All participants reported that the application was easy to use in terms of the design and interface they stated that it was very easy to use from the first day and would be useful to other patients with hand RA.

c) Motivation and adherence: ten participants stated that the smartphone app intervention increased their motivation to exercise their hands. One participant advised, 'I started to do regularly exercise thanks to the application. I want to continue this habit. I would like to use the app if there are exercises for my other joints too.'

They reported that exercise videos, reminders and notifications were their favorite features of the application. One participant said, 'I get the warning that my exercise time is approaching before my training time, this is very useful for me, I do not have to plan or forget it at all.'

Another participant said, 'Reminders and notifications are my favorite, I love that some notifications motivate me by saying 'how about moving? have a nice day!'.

Discussion

The aim of our study is to develop a smartphone application for hand exercises for patients in Turkey with RA and to test its usability. A usable application has emerged with the two-stage process as design/development and usability stages. The design and development stage consisted of two phases. In the first phase, we conducted focus group interview to discuss the content, feature and design of the prototype app. Prototype app consisted of consent, outcome measures, exercise diary and hand exercises. We chose the exercises from the evidence-based SARAH hand exercise programme and adapted them for the mobile application. In phase 2, some notifications were added or modified in the revised version app. A short educational presentation which consisted of steps for using the app was added. Users with RA gave the app high usability scores. The application was found to be easy to use, useful and satisfactory. Our interviews showed that that the app was acceptable to people with hand RA. The app was particularly helpful in teaching patients could learn how to do the exercises correctly. Reminders, notifications, and videos were listed as the favorite features of the app. Participants used the app for different period of time. Some of them only used it for a week or two while others used it for a more extended period. Some of the participants stated that after 2 weeks of using the app, they learned the exercises and felt no need to look to the app. However, these participants still benefited from push-up notifications for reminding them to do their exercises. Use of the app decreased over time.

Previous studies

There are many apps available but few apps for arthritis have been designed by health professionals and patients using an iterative design and development method. Disease-specific applications which are easy to use can support the provision of rehabilitation for patients with long term conditions, such as RA. There are some latest well-designed smartphone applications for assessment of disease-related symptoms and functions [17–19]. However, to date, there are no smartphone exercise apps developed for adults with hand arthritis.

The present project was informed by the results of our previous study [7]. A web-based version of the SARAH programme had been developed previously (mySARAH) to support the performance of the home exercises and to reduce the number of hand therapy sessions. Seven out of eleven SARAH exercises were chosen from the evidence-based SARAH hand exercise programme with a few adaptations for the mobile app.

Strengths and limitations

We have conducted comprehensive testing with input from both therapists and patients unlike many apps that are developed for patients. Testing was over 4–6 weeks of use allowing users time to test it thoroughly. We also tested it across a range of different devices including both IOS ad Android systems. We included participants with a range of different education levels and age groups to ensure it was applicable to a diverse range of patients. A limitation of this study is that we did not assess performance of the exercises to check patients were performing them correctly and we do not know if including modifying the SARAH programme exercises for the mobile app results in the same clinical outcomes as the full SARAH programme. We think that it is very unlikely to affect clinical outcomes, since the change in the adapted exercise program is minimal. Another limitation of this study is that we had hoped to be able to monitor exercise adherence using user activation tracking system, but this would only be possible if patients continued to use the app. Although therapists find the user activation tracking system as beneficial to follow up their patients, it could be also helpful to use patient-reported exercise adherence outcome. Hence, we plan to add a tab to assess the adherence by patient-reported outcome.

Future studies

We have planned a randomized controlled trial which aims to determine the effectiveness of mobile app-based hand exercises for patients with hand RA. During the qualitative interviews, the participants were asked for their recommendations, and many participants suggested an application that included exercises for other joints as well (not just the hand). We plan to add exercises for other joints in our future study. Furthermore, it may be useful to compare web-based and mobile app-based exercise applications in future studies.

Conclusion

A hand exercise mobile app for people with RA was developed using mixed-method and iterative design. The high level of usability and user satisfaction supports the application's utility. It has the potential to be used by health professionals to provide their patients with a personalized home-based exercise regimen, remote monitoring and support exercise adherence.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00296-021-04860-0.

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Author contributions ET, SL and EW conceived funding for the study. ET led the study team. SL was the senior author. ET, EW, CS, and SL contributed to the study design, and drafted and revised the manuscript. FS was involved in study recruitment and ethics approval process. TB and FS assisted in data collection, analysis, and technical works. All authors reviewed and approved the manuscript.

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Declarations

Conflict of interest There are no conflicts of interest to declare.

Ethical approval The study protocol was approved by the Clinical Research Ethics Committee of Marmara University Medical Faculty, Turkey (Number: 06.2019.577).

Informed consent Informed consent was obtained from all participants.

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