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ORIGINAL ARTICLE *Psychology and counselling*

Development, implementation and initial feasibility testing of the MediEmo mobile application to provide support during medically assisted reproduction

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STUDY QUESTION: Is it possible to develop a patient smartphone application for medically assisted reproduction (MAR) that is acceptable to patients and fertility staff?

SUMMARY ANSWER: Staff and patients responded positively to the MediEmo smartphone application, perceiving it to be acceptable and feasible to implement in a busy clinic.

WHAT IS KNOWN ALREADY: Digital tools are increasingly popular to provide practical, administrative and psychological support alongside medical treatments. Apps and other digital tools have been developed for use alongside MAR but there is very limited research on the development or acceptability and feasibility of these tools.

STUDY DESIGN, SIZE, DURATION: Mixed methods research. This article outlines the development phase of the MediEmo smartphone app, which was guided by the Medical Research Council development framework for complex interventions. The resulting MediEmo app was then implemented into a single centre for MAR in the UK, acceptability evaluated and feasibility explored among 1106 potential participants undertaking IVF cycles.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Consultation and data collection took part at a single mid-sized urban fertility clinic. Development of the MediEmo smartphone application took place during 2013 to 2017. Implementation of the MediEmo took place from June 2017 to September 2020. The MediEmo app comprises three functions (six features) namely medication management (medication timeline, messaging), mood management (emotional tracking, coping support) and functional support (frequently asked questions, symptom checker). Data on age, fertility diagnosis, anti-Müllerian hormone level were collected about the users of the MediEmo in addition to MediEmo usage data and attitudes towards the MediEmo smartphone application.

MAIN RESULTS AND THE ROLE OF CHANCE: Informed by the developmental process described, MediEmo is an app combining patient medication diary management and ease of integration into clinic systems with emotional support, emotional tracking and data capture. This study demonstrates acceptability and feasibility of MediEmo, with good uptake (79.8%), mood data sensitivity and reliability and positive feedback.

LIMITATIONS, REASONS FOR CAUTION: Single centre, small number of users in questionnaire studies.

WIDER IMPLICATIONS OF THE FINDINGS: The findings suggest smartphone apps can contribute to fertility care and that patient engagement is high. Evaluation of any apps introduced into clinical pathways should be encouraged to promote development of the most useful digital tools for fertility patients.

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Introduction

Fertility treatment regimens are demanding, with daily hormone injections, ultrasound scans, semen analysis and invasive procedures such as oocyte retrieval (Mahlstedt, 1994; Benyamini *et al.*, 2005). The psychological burden of IVF treatment has been found to be a significant cause of treatment discontinuation (Domar, 2004; Verberg *et al.*, 2008), particularly the experience of an unsuccessful cycle (Gameiro *et al.*, 2012). The 2-week waiting period between an embryo transfer and pregnancy testing in an IVF cycle is known to be particularly difficult, with elevated levels of anxiety (Wischmann, 2008; Boivin and Lancastle, 2010), and patients often require psychological and emotional support during this period of uncertainty. Although the need to provide this support is widely recognized, and in the UK mandated (HFEA, 2019), uptake of existing counselling/support services provided alongside fertility treatments is lower than indicated in intention research (Boivin *et al.*, 1999; Miller *et al.*, 2021) and prospective research (Wischmann *et al.*, 2009). The main reasons for low uptake of counselling are preference for coping with own resources, stigma, uncertainty about what counselling involves and practical concerns such as knowing who to contact, time constraints and cost (Boivin *et al.*, 1999; Benward, 2015). In the era of physical distancing, avoidance of in-clinic contacts and periods of isolation necessitated by the coronavirus disease-19 (COVID-19) pandemic, options for additional remote support may be particularly valuable to patients. Boivin *et al.* (2020), in a cross-sectional study exploring patient's experiences of clinic closures during the COVID-19 pandemic suggest that priority should be given to developing strategies to monitor mental health and provide support so that we can understand the prevalence of poor mental health during medically assisted reproduction (MAR) and the associated patient needs (Boivin *et al.*, 2020). Considering such factors, it has been argued that digital approaches to delivering specific types of patient support should be developed and evaluated to examine their acceptability and feasibility among patients and staff (Meyers and Domar, 2021).

Mobile health (m-health) technologies, such as mobile applications, are increasingly used in other medical contexts, to support patients through complex and emotionally challenging treatments (e.g. Vinehealth, Intellicare) (Lattie *et al.*, 2019). Systematic reviews have demonstrated mobile applications to be effective for mental health (including depression, anxiety, self-injurious thoughts and behaviour) especially as standalone apps targeting-specific conditions (Weisel *et al.*, 2019), and improving well-being and emotion regulation (Eisenstadt *et al.*, 2021). Apps can be accessed by the patient at any time and could therefore be particularly useful in fertility treatment, especially during COVID-19 and during treatment time periods when patients have little or no contact with clinical staff, such as following an embryo transfer. A mobile application could facilitate remote support and treatment adherence in addition to capturing useful data for research, audit and quality improvement purposes. There are fertility digital support tools (Zwingerman *et al.*, 2019), with some specifically developed for use during IVF (Meyers and Domar, 2021). However, IVF-specific support apps are orientated to practical and organizational support features, and none have also focused on emotional demands and been described or evaluated in a peer reviewed study (Robertson *et al.*, 2021). There is a need for objective, transparent and standards-based evaluation of digital health products that can bring greater clarity to the end-user on potential health benefits. This approach therefore needs to be guided by complex intervention frameworks, end-user requirements and formal review on not only technical but also clinical and cost aspects.

The aim of the present study was to examine whether a smartphone application designed to provide remote support to patients during MAR would be acceptable to patient and staff and feasible to implement in fertility clinics. In the study, we report on the steps in the development of the smartphone application, and preliminary process evaluations (feasibility, acceptability and sensitivity) of developing the app.

Materials and methods

Participants

All consultation and data collection took place at a single mid-size urban fertility clinic. The smartphone development period was carried out during 2013 to 2017 and resulted in the MediEmo smartphone application reported on in the present study. The Supplementary Materials and methods report on these phases. The implementation period took place from June 2017 (when MediEmo was introduced) to September 2020 and implementation data are used for data analyses. MediEmo was made available to patients initiating IVF/ICSI cycles, medicated frozen embryo transfer cycles and stimulated IUI cycles, as these cycle types involve medication regimes embedded in the medication timeline of the MediEmo application. To create a homogeneous patient set for whom both the Medi and Emo components of the app would be relevant and for whom usage data could be extracted, patients were only included in the cohort for this analysis if they underwent a stimulated IVF or ICSI cycle and consented for use of their data in non-contact research. Excluded patients were donor oocyte recipients or altruistic oocyte donors or patients undergoing an

oocyte preservation cycle (oncology or social), who would be dealing with more complex psychological issues unrelated to infertility *per se*. Patients undertaking oocyte sharing cycles were included. Usage of MediEmo was not associated with any additional cost to patients. The development data was collected as part of 'service evaluation' to inform the development of a service, and ethical approval was obtained from the University of Southampton and NHS HRA (IRAS 290597) for the collection and analysis of the implementation data. A Data Protection Impact Assessment was approved by the University of Southampton panel on 07 January 2021.

Materials

MediEmo smartphone application

The MediEmo smartphone application was developed to address patient support needs identified through the developmental phase of the research. Development was guided by the Medical Research Council (MRC) development framework for complex interventions (Campbell *et al.*, 2000) that recommends using research evidence and mixed methods data collection with experts and users, to create theory that makes clear the activities and mechanisms of action that lead to intervention impacts on outcomes. Full details of the five phases of MediEmo development are described in the Supplemental Materials and methods and briefly summarized here in Table I. The five phases comprised literature review; consultation with patient and staff regarding desirable features; critical features specification; technical specification; and [beta] user testing. As shown in Table I, Phase I started the process with a review of psychosocial treatment studies, 6 fertility treatment questionnaires, 10 existing IVF apps and inquiry about app usage in 21 UK fertility clinics. A synthesis of these indicated an unmet need for a smartphone application that would address management of both medical and emotional aspects of MAR. In Phase II, consultation with 29 patients and staff in a single centre using mixed methods, identified desirable features (summarized in Supplementary Fig. S1) for patients (e.g. reassuring information, coping techniques, chat forum) and staff (e.g. automated medication timeline, frequently asked questions (FAQs)) that patients perceived would help them feel supported and connected to the clinic, and that staff felt would help patients and make time efficiencies in clinic. As shown in Phase III, not all desirable features could be taken forward due to resources (e.g. appointment system), technical or health and safety requirements (e.g. buddy system) but of those desired, six could be taken forward (e.g. information support, medication and mood management) to technical development. Table II describes these functions according to the Intervention Taxonomy descriptors (Schulz *et al.*, 2010). These comprised three functions (six features) namely medication management (medication timeline, messaging), mood management (emotional tracking, coping support) and information support (FAQs, symptom checker). In Phase IV, the technical group designed and built a secure cloud-based patient portal with registration linking patient and clinic via unique and secure patient identifiers, with synchronized and real-time data according to features described. In Phase V, mixed methods [beta] user acceptance testing showed that patients (26 users) were able to download, register and use the app. Patients most consistently preferred the medication timeline and information features but there was more variation about the messaging, mood monitoring and coping support depending on need and previous treatment experience. Suggestions for modification (e.g. greater clarity on rationale for using app from clinical team) were implemented (when possible). The final version was implemented in the clinic and the version used for implementation data collection.

Mood scores

To evaluate the validity of mood monitoring during the treatment cycles we compared mood scores extracted from MediEmo across stages of the treatment cycle. The mood monitoring embedded in the MediEmo is the emotional reaction list from the daily record keeping (DRK) form (Boivin and Takefman, 1995). The MediEmo emotions list comprises negative (i.e. anxious, tense, nervous) and positive emotions (i.e. confident, positive). In the app, emotions were rated on four-point intensity rating response scales (e.g. 0 = not at all disappointed to 3 = severely disappointed) (see Table II). Average scores for negative and positive emotions were computed. Studies have repeatedly demonstrated that the DRK is sensitive to stages of treatment, with negative emotions increasing (and positive emotions decreasing) significantly during the waiting period due to imminent pregnancy test (i.e. 'imminence effect' (de Klerk *et al.*, 2005; Boivin and Lancastle, 2010)). Data from the app should replicate these reliability and sensitivity analyses if MediEmo is a valid way of accessing patient emotional reactions.

Background information

Data about age, primary infertility diagnosis, anti-Müllerian hormone (AMH) level (pmol/l) of users and potential users of MediEmo were collected from the electronic medical records. These are presented with descriptive statistics.

Usage statistics

Usage data extracted from the MediEmo portal included the number of app downloads, number of patients using the medication timeline and number using the emotional tracking, time and date of usage. 'Using' was defined according to actions taken in the MediEmo app. Using the medication timeline was defined as medication swiped or marked as taken when reminded to take medication by the app. Using emotional tracking was defined as rating any of the emotional reactions when reminded to rate emotions. Patients who downloaded the app but did not use the two key features (but may have used other features like FAQ) were considered passive users, whereas those who declined to download the app were considered non-users.

Attitude to MediEmo

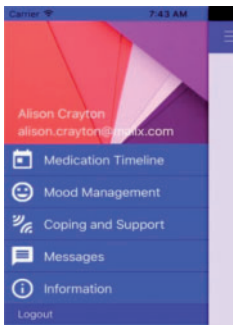
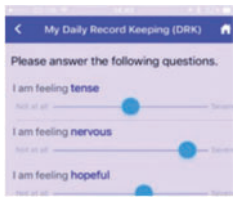
In February 2018 (10 months after implementation began), we electronically pushed a survey to current users on Day 8 of the waiting period, inviting them to rate their attitudes towards the app. Via a push notification, patients received five questions that asked them to rate on five-point bi-polar response scales with anchors the extent to which they perceived the app to be: (i) bad/good, (ii) harmful/beneficial, (iii) unpleasant/pleasant, (iv) worthless/valuable and (v) difficult/easy (Attitude subscale (Ajzen, 1991)). Higher scores (1 to 5) indicated a more positive response. Patients were also asked to type in any additional feedback about MediEmo.

Table I Steps in MediEmo development carried out before the implementation data collection.

Task and aim	Participants	Materials	Outcome
Phase I: Literature review to generate potential concepts for the app based on sources of burden in fertility clinics	Academic psychologists (n = 2) in consultation with clinicians (n = 2), software engineer (n = 1), nurse manager (n = 1)	Psychosocial studies[1] Treatment questionnaires (n = 6)[2] Existing fertility-related apps (n = 10)[3] Inquiry with UK clinics (n = 21) regarding app usage	Decision to focus on medical and emotional management of fertility treatment management and the mobile application format.
Phase II: Consultation with patients and staff to identify desirable components for the app	Patients (n = 17) Staff (n = 12)	Mixed methods approach with rating scales, structured list of features and open text questions	Patients' desirable support features were reassurance, coping techniques, chat forum, buddy-pairing and support call in waiting period. Staff desirable features were automated appointments, medication management FAQs for patients, a trigger for wellbeing check-in to distressed patients in 2-week waiting period. Benefits proposed for these features were patient support and connection to clinic, timely help-seeking and time efficiencies for staff (e.g. reduced phone calls) that could be re-allocated to patient support. Mobile application would help provide 24-h support.
Phase III: Critical features specification	Based on Phase I and Phase II psychologists (Cardiff University) developed the critical features specification that were then reviewed and agreed with the clinical and software engineering members of the technical working group	Technical/resource feasibility of: (i) FAQ/information, (ii) symptom checker, (iii) chat room and buddy system, (iv) appointment management, (v) medication and test result management, (vi) staff and patient communication channel, (vii) treatment stage tracker, (viii) emotion symptom tracker and trigger for calling nurse when distressed, (ix) coping techniques for 2-week waiting, (x) data collection feature and service evaluation.	The following components were taken forward (i) information support (FAQ, clinic and IVF information, symptom checker), (ii) monitoring of medication and mood (medication timeline, appointment schedule, mood tracking), (iii) feedback (reminders, trigger for nurse wellbeing check), (iv) coping support (positive reappraisal coping, distraction, thought challenges) and (v) data collection for service evaluation. Technical needs around onboarding, security and privacy, platform and 24-h access, push notifications, continuous updating, data capture and analytics were also identified.
Phase IV: Technical specification	Technical working group with software engineering team	List of core critical features (Phase II)	Decision to create a secure cloud-based patient portal with registration (app downloaded App Store or Google Play). Portal automatically receives and encrypts patient registration data and links patient and clinic via unique identifier. Data entered (patient, staff) automatically synchronized keeping portal always up to date. Aggregated mood data used to trigger personal response to patient stress.
Phase V: MediEmo user acceptance testing	N = 26 users	Implementation of MediEmo prototype Mixed method consultation, 18 questions about practicality, look and feel and attitude MediEmo	Overall, above average ratings for practicality and look and feel, and attitude towards MediEmo. Most consistently preferred were medication timeline and information features, considerable variation about other features (i.e. messaging, mood management, coping support) depending on need and previous treatment experience. MediEmo prototype amended to address practical issues of implementation and user preferences.

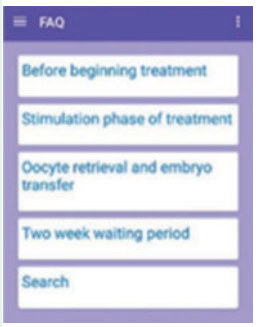
Technical working group involved in all aspects of project development.
FAQ, frequently asked questions.
[1,2]See text for sources consulted.
[3]DrIVF; MyMobileFertility; IVTFertility; FertilityFriend; CinncinnatiFertility; InfertilitySurvivalKit; TheFertilityApp; FertilityView; IVFBabyInTheMaking; iVitro.

Table II Summary of included features (including description by content and delivery characteristics according to Intervention Taxonomy (ITAX)).

Core features	Description	ITAX
Medication timeline 	The medication timeline shows drugs the patients are due to take. Daily reminders specify to the patient the specific times to administer the medication, with prompts to alert the patient to record the drugs administered by either pressing the 'mark as taken' tab on iOS devices or 'swiping' the drug card to the right on Android devices. Overdue medications appear as red, and reminders cease to occur when medication is marked as taken. The clinic is notified drug has been taken.	Content • Provision of individual medication information and notifications/reminders Delivery • Schedule—daily reminder • Scripting—appears after baseline scan when regime assigned during app registration • Sensitivity to patient characteristics—visual symbols used alongside words, but words in English only • Adaptability—programmed to patient-specific regime and adapted by staff during treatment if required according to ultrasound results/clinical judgement
Messages 	If the drug regime alters during the treatment cycle, this change can be communicated by the clinic to the patient via the app in the form of a notification.	Content • Process modification Delivery • Schedule—initiated by clinical team when changes made • Scripting—staff initiated • Sensitivity to patient characteristics—patient cannot amend • Adaptability—patient cannot amend
Mood management 	The mood management domain of MediEmo enables patients to record their daily mood using the daily record keeping form developed for IVF (Boivin and Takefman, 1995; Boivin and Lancastle, 2010). Patients are asked to rate the extent to which they have experienced these emotions on a scale of 0 (not at all) to 3 (severe) using a slider. To avoid overburdening patients, 6 of the possible 15 negative (e.g. feeling tense, nervous) or positive emotions (e.g. feeling hopeful) are randomly presented to patients daily. The mood centre also records whether the patient is experiencing spotting and whether they are experiencing levels of stress they cannot cope with.	Content • Emotional tracking using validated methods for IVF Delivery • Schedule—daily reminder • Scripting—slider enables quantitative responses but elaboration not possible • Sensitivity to patient characteristics—use of slider for ease of input • Adaptability—patient cannot amend emotions
Coping and support 	The coping and support domain provides patients with theoretically derived, positively endorsed coping and support techniques, namely the (PRCI) and a Distraction Based Coping Intervention (DBCI). Instructions on how to use these techniques are provided. The PRCI consists of 10 statements stimulating positive reappraisal of the situation (Lancastle and Boivin, 2008), whereas the DBCI is an emotion focused strategy designed to reduce intrusive cognitions (Bennett *et al.*, 2012) using distraction techniques, e.g. 'Count backwards from a large number in twos', 'Think about a calm place or the sea lapping against the shore'.	Content • Stress management techniques Delivery • Schedule—unlimited, available to patient throughout treatment • Scripting—static educational material • Sensitivity to patient characteristics—users are encouraged to process all material/exercises and perform those that appeal to them • Adaptability—patient decides which (if any) exercises they perform

(continued)

Table II Continued

Core features	Description	ITAX
Information support 	Information about the clinic, the staff and contact details. Frequently asked questions and symptom checker provides information according to treatment phase (i.e. before beginning treatment, stimulation phase, oocyte retrieval, embryo transfer and 2-week waiting period).	Content • Provision of information Delivery • Schedule—available to patient throughout treatment • Scripting—static educational material • Sensitivity to patient characteristics—information cannot be modified by patient • Adaptability—information grouped by treatment type and phase such that patients select relevant information

Procedure

A technical working group was assembled to develop the smartphone application (see Supplemental Materials and methods for procedure at each phase of development). During implementation data collection, every eligible patient undergoing a stimulated MAR cycle was offered the opportunity to use MediEmo. The medical and nursing team explained the clinic rationale for using the MediEmo in terms of its features, namely medication management (timeline and messaging), mood management (mood tracking, coping support) and information support (FAQs and symptom checker) as well as practicality (e.g. ease of use). Patients agreeing to use the app were requested to download the app from Apple Store (iPhone devices) or Google Play Store (Android devices) and provided with a clinic code to register within the app before the start of their cycle. At start-up, the MediEmo app requested patient name and contact information including email address. The app generates a unique user ID to pseudo-anonymize app-collected data. On first opening the app, MediEmo users indicated their agreement to the use of their data for non-contact research to understand how the app was being used and its role in helping patients during fertility treatment.

On the day of the baseline ultrasound scan, when patients attended clinic, the clinical team set-up their cycle regimen (e.g. medication drug, dosage, time of administration) via the MediEmo-Clinic interface. Patients were instructed to start using the MediEmo on the first day of stimulation until the results of the pregnancy test were known. Patients were not given further instructions to use the MediEmo, but medical staff answered any questions about its use. Stimulation was initiated as clinically indicated. When results of the pregnancy test were known, if negative, the cycle medication timeline was deleted from the MediEmo app by the nursing team to prevent any further medication notifications. Patients were still able to record their emotions on a daily basis and access the coping strategies provided in the app if desired. Patients were able to continue to use all features of the MediEmo app after a positive HCG pregnancy test, with ongoing reminders to take their progesterone medication.

Data analysis

Data from the mood management and medication timeline features were extracted from the MediEmo app platform and then linked to clinical data from the electronic IDEAS^{TM} (Mellowood Medical) database using the patient's hospital ID number. After linkage, the resulting study database was fully anonymized and analysed using R software (R Core Team, 2014). Descriptive statistics were used to examine MediEmo usage relative to the day of egg collection. Cronbach coefficient alpha was used to examine internal consistency (i.e. reliability) for the negative and positive emotions. Values <0.70 were considered questionable or poor, 0.70 to 0.80 acceptable, between 0.80 and 0.90 good, and >0.90 excellent (Ponterotto and Ruckdeschel, 2007). To explore sensitivity of the app to treatment stage negative and positive emotion scores pre- and post-day of egg collection were compared. The unit of analysis for this comparison was the cycle (rather than patient) because not all patients entered data daily for the duration of their cycle. Any cycle days with <10 individuals entering mood data were excluded from analysis. A mixed linear model was used to compare mood data pre- and post-oocyte retrieval, to account for variable numbers of days of emotional tracking.

Results

MediEmo usage

During the implementation period (June 2017–September 2020), 1106 unique patients meeting the inclusion criteria undertook at least one IVF cycle in the centre. Figure 1 shows the pattern of uptake for MediEmo. Of eligible patients, 883 patients (79.8%) used the medication timeline and 685 patients (61.9%) used both the medication timeline and emotional tracking during their IVF/ICSI cycle. All app users used the medication timeline, and none of the users used only emotional tracking.

A total of 223 patients (20.1%) were non-users. Most of these were passive users ($n = 195$), who were recorded as agreeing to use the

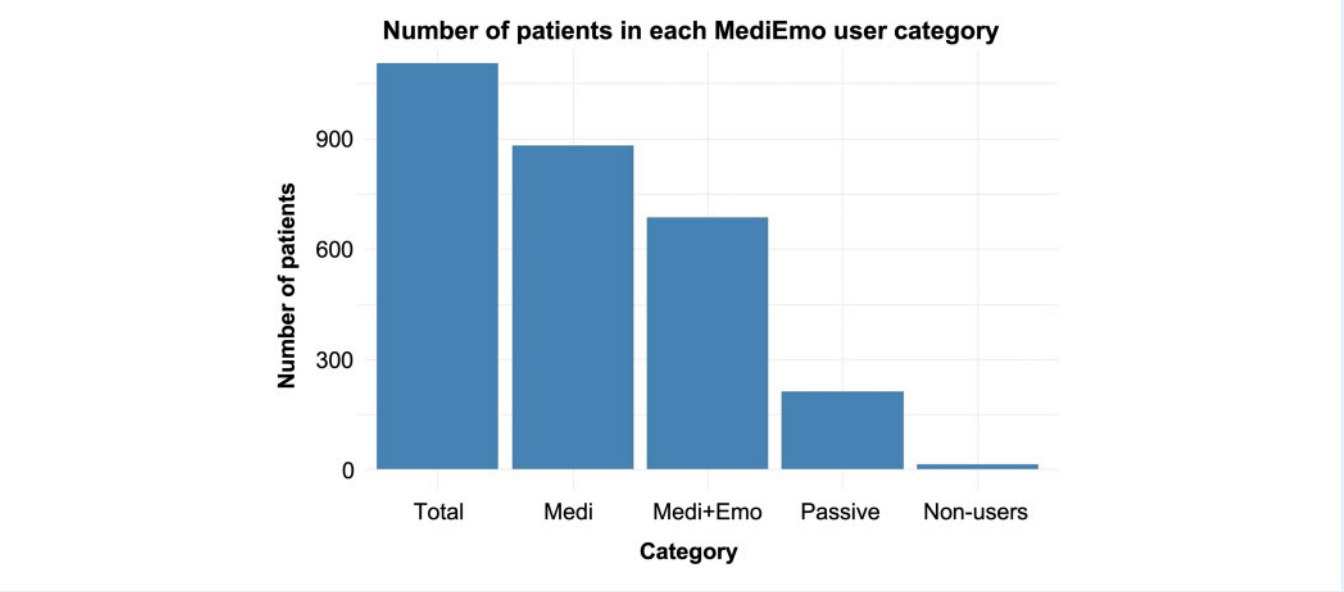


Figure 1. Bar plot of patients in each user category, showing total potential user cohort, number using medication timeline only (Medi), number using medication and emotional tracking (Medi + Emo), passive users who downloaded the app but did not use it and those who declined to use the app (non-users).

app within their medical notes but did not use the MediEmo during their cycle. These patients had consented to app use in their nurse cycle-planning consultation, downloaded the app, and had their cycle information (e.g. medication drug, dosage, time of administration) set up by the clinical team. However, they never responded to reminders from the medication timeline or emotional tracker. A total of 28 patients (2.5% of eligible) declined to use the app when invited. Of those with an explanatory reason recorded in their clinical notes, the reasons cited were language barrier (n = 4), learning disabilities (n = 2), mobile phone unsuitable or too old (n = 5) and preferring telephone voice call communication (n = 10).

Users had a mean age of 32.7 years (*SD* = 4.45). Patients who did not use MediEmo had a mean age of 33.9 years (*SD* = 4.63). Mean AMH was 23.5 (*SD* = 22.2) pmol/l for app users and 21.5 (*SD* = 19.3) for non-users. The three most common primary infertility diagnoses were unexplained, male factor and ovulatory disorders in both the user group and the group who did not use the app.

The median number of days between cycle start and egg collection date was 13 (interquartile range 11–14). Amongst the 883 patients who used the medication timeline feature, 79.4% marked ≥1 stimulation medication dose as taken during their IVF cycle. The total number of days patients recorded medications as taken (either by pressing the 'mark as taken' tab on iOS devices or 'swiping' the drug card to the right on Android devices) is summarized in Table III. Overall, 56.2% (n = 4547) of the individual stimulation medication doses scheduled in the app (e.g. Gonal F/Menopur) were marked as taken by a MediEmo user. The proportion of scheduled progesterone supplement medications/pessaries that were marked as taken in the app was higher (70.6%, n = 23 347 of total 33 070 progesterone medications scheduled in MediEmo medication timeline).

Table III Break down for number of days of engagement per participant for medication timeline component.

Number of days medication timeline used	N (number of Medi medication timeline users)	% of Medi users (n = 883)
1–2	112	12.7
3–5	27	3.1
6–8	31	3.5
9–11	27	3.1
12+	686	77.7

Of the users using emotional tracking, most tracking was done during the stimulation phase of the IVF cycle, with fewer patients tracking their mood into the 2-week wait phase (see Fig. 2).

Mood data reliability and sensitivity

Cronbach reliability coefficient alpha for negative emotions (coefficient alpha = 0.83 (CI 0.79:0.85), n = 778) and positive emotions (coefficient alpha = 0.88 (0.86:0.90), n = 756) were above the 'acceptable' cut-off (i.e. ≥0.70).

Figure 3 shows negative emotions across stages of the IVF/ICSI cycle. As can be seen negative emotions increased after oocyte retrieval whereas positive emotions decreased. A mixed linear model, including random effects grouping factors of patient id and mood name, showed that stage of cycle (pre- versus post-oocyte retrieval) was significant in

predicting entered mood scores ($P = 0.037$, SE 0.012, df 12.5). We used R (R Core Team, 2014) and lme4 (Bates et al., 2015) to perform a linear mixed effects model analysis of the relationship between mood score and the day in cycle relative to egg collection. These models were significant ($P < 0.001$), with a trend of −0.0176 (CI −0.019: −0.0154) change in positive emotion rating/cycle day and a 0.0179 (CI 0.0104:0.0192) increase in negative emotion rating per cycle day, after accounting for between participant variation in mood score ratings.

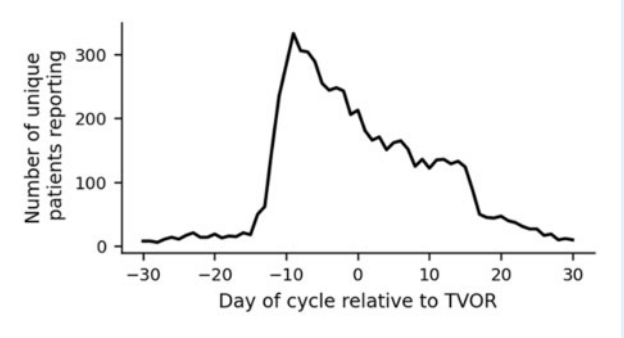


Figure 2. Usage pattern of MediEmo emotional tracking during IVF/ICSI. Day of cycle refers to the day in the IVF cycle emotional data was entered on relative to egg collection/transvaginal oocyte recovery day (TVOR day = 0).

Attitude to MediEmo

In total, 97 of the 138 active app users in January–March 2018 responded (70.3%) to the attitude survey and rated the attitude statements to the MediEmo app on Day 8 post-transfer (see Fig. 4). Overall, the app was rated positively (overall $M = 4.66$, $SD = 0.63$).

Few users (17.5%) provided textual feedback. Most feedback reinforced the quantitative scores (e.g. 'Easy to use and good reminder of medications') but a few referred to setting preferences for notifications e.g. when medication could be marked as taken. Additionally, some suggestions for improvements were also made, e.g. 'on the mood graph would be beneficial to add physical symptoms'.

Discussion

We have demonstrated that it is possible to develop a smartphone application for patients to use during MAR that is acceptable to patients and staff, and feasible to implement in a mid-size fertility clinic in the UK. MediEmo was developed according to the MRC framework for developing complex interventions (Campbell et al., 2000; Aarts et al., 2012; Craig et al., 2013). Patient users were involved in the development of this tool from the very earliest phases of app design. We have presented here the development process, initial

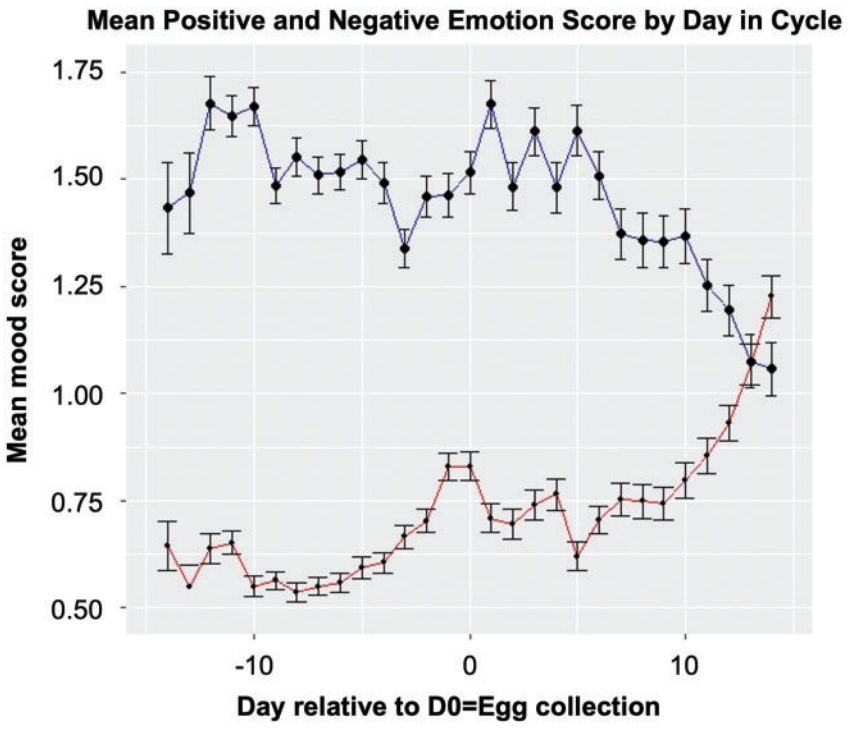


Figure 3. Mean negative (red) and positive (blue) emotion scores (±SEM) from day −14 to +14 from day of egg collection.

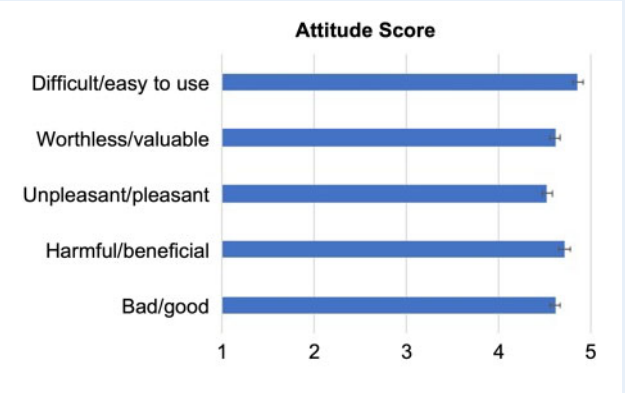


Figure 4. Mean attitude score for each attitude statement (±standard error bar). Higher scores indicate more positive attitudes.

implementation usage data (feasibility and acceptability) and psychometric properties (reliability and sensitivity) which together provide promise for use of m-health tools in MAR. The next steps in development comprise an examination of the association between active app usage and clinical outcomes, in preparation for an efficacy evaluation study.

Strengths and limitations

The limitations of the development and implementation should be considered. One limitation of the present study was that a formal systematic review of existing IVF apps was not undertaken at the initial time of development. While this could have missed important contributions, a subsequent systematic review carried out on IVF-specific apps showed similar gap in digital support as we concluded at the time (see Robertson *et al.*, 2021). The consultation of patients and staff occurred in a single centre, in iterative samples of fewer than 20 people. Consultation therefore may not reflect the views of all patients at this or other centres and may provide more of a broad outline of patient support needs (medical and emotional management) than its finer details. However, our review of treatment questionnaires, treatment difficulties studies and IVF apps of the time identified desirable components that were consistent with those identified in our patient and staff consultation. In developing future digital support apps, multicentre approaches could be warranted if apps are to be disseminated more widely. We had a multidisciplinary technical development team (psychologists, medical staff and software engineers) that informed choices about app design and features. It would also have been useful to have design experts who could have helped with decisions about how best to onboard patients to the app or create a 'look and feel' from user design perspectives. We were not able to examine usage of the non-interactive components of the app (i.e. information support such as symptom tracker, FAQs), or to examine rationale for non-usage. It was noted in medical records that some non-users (i.e. not interacting with app) nevertheless reported they were 'keen to use MediEmo again' when they returned for another IVF cycle, suggesting that passive users may benefit from MediEmo without entering any data into it. For example, having the medication regime displayed in the app timeline could be a useful reference point, or reassurance from reading FAQs. These findings reflect the challenge of studying app engagement, and it may be that the number of logins or pages viewed, or notifications acknowledged would be useful additional variables to evaluate app usage more accurately.

Overall patients were positive about MediEmo and were willing to use it. Ninety-eight percent of eligible patients expressed willingness to use the app, and almost 80% did so. High uptake compared to other apps indicates an unmet need for digital support that combines medical and emotional aspects of treatment, as suggested in previous reviews (Meyers and Domar, 2021). Users gave moderately positive ratings (see Supplementary Materials and methods) with some potential areas to improve the app, for example the onboarding process. The main issues captured in people declining to use the app (<3%) related to inclusivity, namely issues around ethnicity (i.e. language), disability and technology poverty (i.e. type of phone). COVID-19 has made very evident the digital divides within the population, from structural (e.g. broadband speeds, types of phones) to individual issues (e.g. health literacy skill), despite digital apps also widening access (Blacklow *et al.*, 2021). While MediEmo shows promise in widening reach and access to potential sources of support during MAR because it is digital, more resources need to be allocated to making it more inclusive of the MAR population, for example, through translation and inclusion of non-verbal images or animations. Moreover, implementation of the MediEmo across countries and clinics would need to consider and accommodate technical variations in terms of user ability and clinical systems.

Patients have preferences about the different app components and those preferences may produce variable usage across the treatment cycle. The features of the MediEmo app were selected based on theory, empirical research and consultation with patients and staff about desired support. However, acceptability and feasibility data suggested a stronger preference for medical than emotional management components. More cycles showed evidence of the medication timeline being used (80%) than the emotional tracking (62%) and patient and staff consulted about the app gave more favourable perceptions to medical management. It is unlikely that the observed pattern of usage of the emotional tracking feature during the early part of the cycle is due to greater burden of stimulation over burden of waiting period, given existing findings about waiting for pregnancy test results (Benyamini *et al.*, 2005). Drop-off in MediEmo usage after oocyte retrieval could simply reflect typical attrition observed with mHealth interventions in ART (van Dongen *et al.*, 2016; Bernd *et al.*, 2020). Alternatively, the differential between medical and mood management component use could reflect societal attitudes and individual differences in relation to psychological support, which are well established. Most patients prefer to cope with treatment using their own coping resources (e.g. own resilience, support from family and friends) and only about 10–15% use face-to-face counselling when it is offered as part of standard care (Boivin *et al.*, 1999) though higher uptake (34%) is possible with more motivated offers (e.g. research incentive (Wischmann *et al.*, 2009)). Against this counselling usage, it could be argued that the comparatively higher usage for the MediEmo emotional tracker could in fact indicate that MediEmo was indeed successful in addressing an unmet support need. A 'self-help' resource might possibly be more easily used to augment other sources of patient support or coping resources

than other types of resources. The limited consultation sample sizes did not allow for meaningful analysis of individual differences on usage, but such moderator analyses could be the subject of future studies on digital support health apps.

Digital health technology development is an ongoing process that does not end with creation of the technology. More patient support tools, tackling other crucial issues in treatment need to be developed (e.g. treatment planning and continuation (Harrison *et al.*, 2021)). The development of digital tools in accordance with the MRC framework, as per MediEmo development, and their evaluation against patient outcomes in randomized trials, should be encouraged. Rigorous development and evaluation would drive innovation, reduce research waste, encourage uptake of useful tools and ultimately, improve outcomes for patients as shown in other health domains using digital technologies (Lattie *et al.*, 2019). Medical apps and other digital tools are now widespread, with some marketed directly to patients and others recommended or prescribed by clinicians. The research evidence supporting medical apps is extremely limited compared to the number of apps developed and available for use (Byambasuren *et al.*, 2018). Conversely, many tools developed and validated in research studies fail to achieve widespread clinical implementation (Gordon *et al.*, 2020). Apps and tools for fertility patients are prevalent and widely used, but they are variable regarding the theory or user consultation underpinning their development. Furthermore, recent reviews have demonstrated that very few available tools are supported by research evidence (Meyers and Domar, 2021; Robertson, 2021). Only a handful of available general infertility apps have any efficacy data at all (e.g. Domar, 2019; Kruglova *et al.*, 2021), with almost no randomized controlled trials. The limited available research data has demonstrated that apps can increase fertility knowledge and awareness of fertility risk factors, but have not shown a significant benefit of app usage on anxiety, depression or fertility problem index scores. The psychometric analyses in the current research showed that emotional tracking with MediEmo replicated well-established findings of reliability and the imminence effect (Boivin and Lancastle, 2010) which is good evidence for its use as a sensitive data collection device to support further patient support and research evaluation. However, future research, like that of research with general infertility apps, needs to also demonstrate its benefits to patient wellbeing and clinical outcomes using appropriate research methods (e.g. randomized controlled trials, and real-world evidence).

While the current results demonstrate the MediEmo to be acceptable and feasible to implement, we do not yet know whether the MediEmo is perceived as helpful or supportive for patients during MAR. The next development steps with MediEmo will therefore be to focus on optimization and evaluation. Iterative improvement of MediEmo, with involvement of patient users in co-production of any new features, is likely to optimize app development. An evaluation study is in progress, comparing the clinical outcomes of MediEmo users and non-users (active, passive and non-users) to examine whether the MediEmo is a valuable additional source of support during MAR. The rates of return for further IVF treatment after a failed initial first complete cycle of treatment will be evaluated because MediEmo is intended to achieve positive clinical outcomes through reducing burden-related drop-out from fertility treatment.

Conclusion

In conclusion, we demonstrated that it was possible to develop a smartphone application that was acceptable, feasible and designed to support patients and staff manage medical and emotional aspects of fertility treatment. The selection of app content was informed by existing research on psychological support during IVF/ICSI and patient and staff consultation in line with the MRC framework. Ongoing work is focused on optimization of the app and evaluation of the extent to which MediEmo achieves the aim of providing much needed additional practical and psychological support during fertility treatments.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Authors' roles

I.R.: data collection and analysis for implementation and feasibility study; manuscript writing addressed revisions and final write-up. C.H.: member of the technical working group (Phases I to V), development and data collection (designed mixed methods data collection, interpretation, synthesis for specification, specification development), drafting supplemental methods and manuscript, addressed revisions and final write-up. Y.C.: contributed to development and implementation work, data interpretation and manuscript writing, addressed revisions and final write-up. K.Y.B.N.: contributed to data collection and analyses for the implementation study (reliability and sensitivity data). Contributed to the manuscript. N.M.: involved in initial development work, contributed to manuscript. J.B.: led the technical working group (Phases I to V), together with C.H. ran the development data collection (designed mixed methods data collection, interpretation, synthesis for specification, and drafted the supplemental methods); together with Y.C. and I.R. designed the implementation data collection, assisted with data interpretation and drafted manuscript, addressed revisions and final write-up.

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Conflict of interest

Outside of the submitted work, J.B. reports personal fees from Merck KGaA, Darmstadt, Germany, Merck AB an affiliate of Merck KGaA, Darmstadt Germany, Theramex, MedThink China, Ferring Pharmaceuticals A/S, grant from Merck Serono Ltd, outside the submitted work and that she is co-developer of Fertility Quality of Life (FertiQoL) and MediEmo app; N.M and C.Y are minority shareholders

and J.B.'s University (Cardiff University) owns one third of shares. None of the shareholders benefitted financially from MediEmo. I.R., C.H. and K.Y.B.N. declare no conflicts of interest.

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