Observational cohort study exploring MediEmo smartphone application use, live birth, and in vitro fertilization treatment return rates

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Objective: To explore the associations between the use of the MediEmo smartphone application and in vitro fertilization (IVF) live birth and treatment return rates.
Design: A 3-year observational cohort study
Subjects: Patients undergoing IVF were classified as users if they used the medication or emotion features of the MediEmo. Patients who did not use the two key features or declined to use the application were classified as nonusers.
Exposure: The use of the MediEmo smartphone application.
Main outcome measures: Outcomes of interest were the rate of live birth per fresh index cycle, live birth per complete cycle, and treatment return for a stimulated cycle of treatment within 12 months of the unsuccessful stimulated index cycle.
Results: A total of 1,081 patients were eligible to use the MediEmo application, 863 were categorized as users and 218 as nonusers. MediEmo use was associated with a higher live birth rate per index cycle than nonusers (27.81% [n = 240/863] vs. 19.26% [n = 42/218], respectively, OR, 1.248; 95% CI, 1.041–1.509) and treatment return rate compared with nonusers (46.00% [n = 169/363] vs. 31.37% [n = 32/102], respectively, OR, 1.339; 95% CI, 1.092–1.656). It was not associated with the live birth rate per complete cycle.
Conclusion: The observed positive association between MediEmo use and live birth and treatment return rates suggests benefits to patients and clinics. Further research and replication using a randomized controlled trial design are warranted, as is investment in the development of digital tools for use during IVF treatment. (F S Rep® 2025;6:159–65. ©2025 by American Society for Reproductive Medicine.)

Key Words: MediEmo use, treatment return rate, live birth rate

Digital tools such as smartphone applications are increasingly used alongside medical treatments. Numerous mobile applications have been developed for in vitro fertilization (IVF) settings, but most provide practical, lifestyle, or administrative support only, and few are supported by research evidence (1–3).

The MediEmo smartphone application was designed to provide remote practical and emotional management during fertility treatment (4), but also to be applicable for use during any

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medical treatment that includes both a complex medication regime and medical waiting periods, e.g., waiting for a pregnancy test. Features of the MediEmo include a medication timeline that automatically sends notifications to the patient to prompt medication administration according to the patients' medical regime, a mood management component that enables (and prompts) daily emotional monitoring using items from the daily record keeping form validated in IVF (5) and evidence-based coping tools (6, 7). The application also incorporates information support (e.g., frequently asked questions [FAQs], symptom checker) that patients can access at any time (MediEmo features Table 2 in Robertson et al., 2022, (4)).

Initial development, implementation, and feasibility data have shown the acceptability and feasibility of implementing the MediEmo in fertility clinics (4). Results from this research demonstrate that patients have high engagement with, and positive perceptions toward the application, particularly the medication timeline. Further, emotional data (i.e., negative and positive emotion scores) collected by the application showed high internal reliability and replicated previous research that shows a pattern of emotional responses (i.e., emotional signature of IVF) experienced during fertility treatment, including the imminence effect of intensified negative emotions as the pregnancy test approached (e.g., (5, 8)).

Reliable digital tools, resources, or interventions have been suggested to have the capability to change assisted reproduction, patient experiences of treatment, and treatment success rates (3). Given the psychological burden of fertility treatment contributes to treatment postponement and discontinuation (9–11), the use of digital tools such as the MediEmo, which provides patient-level support through the incorporation of evidence-based resources, in addition to practical and administrative support, could help advance these suggestions further. Moreover, exploring the use of such tools could advance research into the associations between use, treatment continuation, and treatment outcomes (e.g., live birth rates [LBRs]).

The aim of the present observational cohort study was to capture real-world data on the uptake and use of MediEmo to prospectively estimate the association between application use (users vs. nonusers) and the clinical outcomes of live birth and treatment return rates. Based on previous research, we hypothesized a positive association between application use and clinical outcomes, namely higher return and LBRs in MediEmo users than in nonusers.

MATERIALS AND METHODS

The MediEmo study procedures have been described previously (4) but are summarized here. Reporting was according to the STrengthening the Reporting of OBservational studies in Epidemiology checklist for cohort studies.

Participants

Data were collected during the implementation of the MediEmo at a single center from May 2017 (when MediEmo was introduced in the clinic) to September 2020. MediEmo was made available to patients undertaking cycle types with medication regimes suitable for input into the medication management component of the MediEmo application, e.g., medicated frozen embryo transfer and stimulated intrauterine insemination. However, for this study, only patients undertaking IVF/intracytoplasmic sperm injection (ICSI) cycles with a plan for fresh embryo transfer were included. Patients undertaking egg sharing cycles (n = 8) were excluded. All participants were asked to give their consent for their data to be used in the current noncontact medical research. Ethical approval for this study for the collection and analysis of implementation data was obtained from the University of Southampton and National Health Service Health Research Authority (IRAS 290597).

Materials

MediEmo smartphone application. As reported previously (Table 2, in Robertson et al., 2022) (4), MediEmo comprises 3 core components (6 features), namely medication management (timeline and messaging), mood management (mood tracking and coping support), and information support (FAQs and symptom checker). All data inputted into the MediEmo are held securely in an encrypted, cloud-based portal (full development details and Supplementary Materials and Methods (4)).

Measures

MediEmo usage. Patients were assigned to the user group ("users") if they used either the medication timeline or emotional tracking features of the application. Patients who downloaded the application but did not use either of these two key features (but may have used other features such as FAQs) or declined to use the application were assigned to the nonuser group ("nonusers") (Robertson et al. 2022(4)).

Participant demographics and treatment characteristics. The participant demographics and treatment characteristics data collected from the clinic database for use in this linkage analysis included patient age, antimullerian hormone (pmol/L), cycle number, cycle outcome (number of live infants per cycle, and live birth [yes/no] per initiated cycle, and per complete cycle), number of eggs collected, and embryos cryopreserved and diagnosis.

Clinical data

Treatment return rates. Treatment return rate was the proportion of patients, expressed as a percentage, of patients who returned and started another stimulated fresh cycle of treatment within 12 months of the failed index cycle of their complete cycle. A complete cycle was defined as all embryo transfers, including frozen, resulting from one episode of ovarian stimulation.

Live birth rate. "Live birth" (yes/no) was defined as a live-born neonate. "No live birth" included IVF/ICSI cycles that were cancelled midstimulation, those with failed fertilization, no embryos for transfer, failed implantation after embryo transfer, or pregnancy resulting in miscarriage.

Procedure

At their precycle nursing consultation, patients were informed how to download the application from the Google Play Store (Android devices) or Apple App Store (iPhone devices) to their smartphone and create a user account. Their profile was then populated with relevant medication information via the clinic portal, through which medication changes could also be made during the treatment cycle, as necessary.

Data analysis

Data from the emotional tracking and medication timeline features were extracted from the MediEmo application platform and then linked to the clinical data from the clinic's electronic patient database IDEAS (Mellowood Medical) using the patient's hospital ID number. After linkage, the resulting study database was fully anonymized and analyzed using R software (12). For LBR and treatment return rates, data for the index and subsequent linked cycles (where relevant, e.g., subsequent thaw transfers) were used.

To examine the association between MediEmo usage and the clinical outcomes, the user and nonuser groups were compared on clinical variables specifically LBR per fresh index cycle; LBR per complete cycle; and return rates for a stimulated cycle within 12 months of an unsuccessful stimulated index cycle from a complete cycle of treatment. By a complete cycle, we mean all fresh and frozen embryo transfers resulting from one stimulated cycle of treatment. For the complete cycle analysis (LBR per complete cycle), cycles not yet yielding a live birth but having remaining frozen embryos in storage were excluded from analysis because the cycle was not yet complete. For the return rate analysis (return rates for a stimulated cycle within 12 months of an unsuccessful stimulated index cycle from a complete cycle of treatment), only patients who had a failed complete cycle, i.e., had used all embryos generated from their index egg collection and for whom the initial fresh index cycle was more than 1 year ago were included as per definition of treatment discontinuation in a previous systematic review (13). Cycles with remaining frozen embryos or where the original fresh index cycle was undertaken less than one year ago were excluded from this analysis because the cycle was not complete or insufficient time had elapsed to meet the Gameiro et al. (2013) (13) definition of discontinuation. Previous analysis has demonstrated this approach will capture 92% of those who return for a further fresh stimulated cycle within this center (14). Statistical comparison between users and nonusers was performed using the Wilcoxon's rank sum test because the data was not normally distributed or the X^2 test (as appropriate). Associations between clinical variables (live birth and return rate) and MediEmo use, controlling for confounders (i.e., demographic characteristics), were further examined using logistic regression. The full interaction model (model 1) was fit first and included age as a potential confounder, MediEmo use, and the interaction between age and MediEmo use to examine whether it moderated any significant association between MediEmo use and outcomes (live birth or return rate). Model 2 included age and MediEmo use only, without interaction. The final model, model 3, included only the age to examine whether removing MediEmo use significantly reduced the fit of the model predicting the outcome. The decrease in fit between models was examined using likelihood ratio tests with *P* values and the Akaike Information Criterion (AIC). The AIC is a measure of fit (penalized for the number of parameters i.e., variables in the model); a lower value is a better fit. Continuous confounders were centered, and effects coding was used for dichotomous predictors. Odds ratio (OR) and 95% confidence interval (CI) were reported. The criterion for statistical significance was $P < .05$.

RESULTS

MediEmo application use

Of 1,280 patients seen in the clinic, 1081 were eligible to use the MediEmo application for a fresh stimulated cycle, and of these, 863 were categorized as users and 218 as nonusers. All the users used the medication management component, and none of the users used only the emotional tracking. The median number of days of emotional tracking during the treatment cycle was 6, with a mean of 8.73 days (standard deviation 8.74). Usage of the medication management component of MediEmo showed 12.7% using the medication timeline on just 1 or 2 days and 77.7% on 12 days or more (Table 2 in Robertson et al., 2022(4)).

Patient demographics and treatment characteristics

Table 1 shows descriptive and inferential statistics for patient demographics (i.e., age), treatment characteristics, and clinical outcomes according to user group. MediEmo users were significantly younger than nonusers, and users included fewer people with social infertility than nonusers. The user groups did not differ significantly on the number for whom it was a first IVF cycle at the center, antimullerian hormone, number of eggs collected, or number of embryos cryopreserved. For clinical outcomes, there was a significantly higher LBR in MediEmo users than nonusers in the stimulated index cycle, but the LBR per complete cycle was not significantly different between groups (Supplemental Table 1 (available online) for further detail on cycle outcome according to user group).

Use of MediEmo application is associated with live birth on the index cycle and treatment return rates after the index cycle

Supplemental Tables 1 and 2 (available online) show results of model testing with logistic regression for live birth resulting from a stimulated index cycle and treatment return rates, respectively. The logistic regression for LBR (Supplemental Table 1), controlling for age, showed MediEmo use was significantly associated with live birth on the index cycle (OR, 1.246; 95% CI, 1.040–1.507) when controlling for age, and the interaction between age and MediEmo use (model 1). The interaction (age X MediEmo use) was not significant (OR, 1.009; 95% CI, 0.969–1.051) in model 1, which means there was little evidence that age of participants moderated the significant association between MediEmo use and live

TABLE 1

Descriptive and inferential statistics for patient demographics, treatment characteristics, and treatment outcome data for MediEmo users and nonusers.

Variable	Users (n = 863)	Nonusers (n = 218)	Wilcoxon's rank sum test/χ^2 for binary values, *P* value
First IVF cycle at this center, % yes (n)	86.91% (750/863)	87.61% (191/218)	.869
Age, y, mean (SD)	32.80 (4.43)	33.89 (4.63)	.001
Diagnosis % (n)			.007
Female factor	30.36 (262)	29.36 (64)	
Diminished ovarian reserve	4.29 (37)	5.05 (11)	
Male factor	24.33 (210)	23.85 (52)	
Severe male factor	3.01 (26)	2.29 (5)	
Unclassifiable/other	.35 (3)	0.46 (1)	
Unexplained	30.48 (263)	23.39 (51)	
Social infertility	7.18 (62)	15.60 (34)	
AMH (pmol/L) mean (SD)	23.59 (22.43)	21.34 (19.48)	.421
No. of retrieved oocytes mean (SD)	12.07 (8.30)	11.68 (8.32)	.472
No. of embryos cryopreserved mean (SD)	1.77 (2.55)	1.73 (3.02)	.418
Live birth rate (LBR) per cycle started, % with live birth	27.81% 240/863	19.26% 42/218	.013
LBR per complete cycle, % with live birth (n)	46.32% 359/775	38.78 76/196	.069
Return rate for repeat fresh cycle within one year after a failed complete cycle of treatment, % yes (n)	46.56% 169/363	31.37% 32/102	.009

Note: All values to two decimal points except *P* values.
SD = standard deviation; AMH = antimullerian hormone; LBR = live birth rate.

Robertson. MediEmo, IVF live birth and return rate. F S Rep 2025.

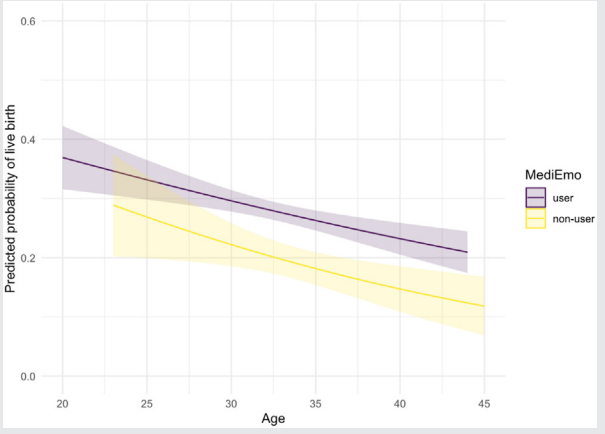
birth. Eliminating MediEmo use from the model (model 3) produced a significantly worse model fit (P=.016) and an increased AIC (+3.807) from model 2. The best-fitting model by AIC was model 2, with MediEmo use remaining significant after controlling for age (OR, 1.2484; 95% CI, 1.01–1.509). Figure 1 shows the predicted probability of live birth for MediEmo users and nonusers according to age. It was not possible to control for diagnosis using fixed effects logistic regression because of multiple diagnostic cell sizes < 5. However, controlling for diagnosis using a generalized linear model showed no marked effect of diagnosis on results reported here (Supplemental Table 3, available online).

Logistic regression for treatment return rate (Supplemental Table 2), showed MediEmo use was significantly associated with returning for a further stimulated cycle within one year of a failed stimulated index cycle. The best-fitting model for return rate was model 2, which showed MediEmo use to be significantly associated with a higher return rate controlling for age (OR, 1.339; 95% CI, 1.092–1.656). The interaction between age and MediEmo use was not significant (OR, 1.008; 95% CI, 0.964–1.052). Removing MediEmo use from the model significantly decreased the fit index (P=.005) and increased AIC (+5.96). Figure 2 shows the probability of returning for MediEmo users and nonusers according to age. As with LBR it was not possible to control for diagnosis using fixed effects logistic regression because of multiple diagnostic cell sizes <5. However, controlling for diagnosis using a generalized linear model showed no marked effect of diagnosis on results reported for return rate (Supplemental Table 4, available online).

DISCUSSION

MediEmo use was associated with a higher LBR (per fresh index cycle) and a higher rate of return for further fresh IVF treatment after an initial failed cycle of treatment, after controlling for age, compared with nonusers. This finding

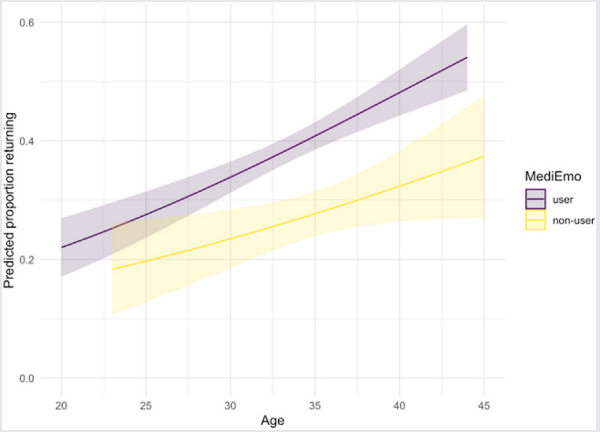
FIGURE 1



The probability of live birth per fresh index cycle for MediEmo users and nonusers controlling for age. Color indicates MediEmo use (*purple* = users, *yellow* = nonusers), width of shading around each line indicates standard error of the estimate of the predicted probability.

Robertson. MediEmo, IVF live birth and return rate. F S Rep 2025.

FIGURE 2



The probability of returning rate within 12 months of a failed fresh (index) cycle for MediEmo users and nonusers controlling for age. Color indicates MediEmo use (*purple* = users, *yellow* = nonusers), width of shading around each line indicates standard errors of the estimate of predicted probability.

Robertson. MediEmo, IVF live birth and return rate. F S Rep 2025.

suggests MediEmo use could have benefits on clinical outcomes beyond simple tracking that need to be investigated with appropriate randomized designs in future research. These findings suggest that engagement with mobile applications should be supported. However, replication is needed considering factors not controlled in the present study.

The positive association between MediEmo use and clinical outcomes is in keeping with the MediEmo logic model, but the use of an observational design means other uncontrolled factors associated with application use and clinical outcomes could explain this association. Many system and individual characteristics have been associated with the uptake of digital resources (e.g., accessibility, cost, trust, digital literacy, attitude toward technology, and cognitive ability) (15). Our previous reports indicate that reasons for declining to use the application (2.5% of those eligible, n = 28 (4)), were related to a language barrier, disability, unsuitable or old mobile phone, and preference for a telephone call, supporting these general findings. Probably the most relevant of these to the clinical outcomes are age, ethnicity, and socioeconomic status (15) because these have been shown to be associated with the probability of pregnancy or return rates (16). The clinic did not record ethnicity or socioeconomic level, and these would need to be investigated in future research because such differences may exist. For example, we did find more cases of social infertility in the nonuser group than the user group, and this may be because people using fertility treatment for social reasons (e.g., same sex couples and single people) often do not perceive themselves as infertile. As such, they may not feel the same need for the MediEmo digital resource as other people with biological problems blocking their fertility. We do not think this would explain the association between MediEmo use and clinical outcomes, because the reverse would be expected; those seeking treatment for social reasons (i.e., those without biological problems) might be expected to have higher, not lower, fertility rates than other diagnostic groups.

In the present study, users and nonusers did not differ on experience with the IVF center, ovarian reserve marker, and treatment characteristics (e.g., number of eggs collected and cryopreserved embryos). Users were younger than nonusers, but the association between MediEmo use and clinical outcome remained after controlling for age. It also remained significant when we controlled for age as a moderator, indicating that the association was not simply because of younger ages using the application more than older ages. Controlling for diagnosis also did not change the results reported. Although confirmatory research is needed, the results suggest that MediEmo application use could confer benefits beyond practical medication and mood tracking, which need to be investigated in future research alongside a more in-depth examination of other potential confounders. A randomized controlled trial (RCT) and process evaluation could examine efficacy and point to which aspect of the application (e.g., medication reminders, mood tracking, and information) is most associated with benefits to elucidate fully the determinants of the association between the use of the MediEmo application in fertility care and clinical outcomes.

According to the MediEmo logic model (Supplemental Fig. 1, available online), the positive associations between use, live birth, and treatment return rates could be the result of using the different components of the MediEmo application. The link between the psychological burden of treatment and treatment discontinuation is well established (11). Therefore, use of the mood management component and its associated coping and information resources, which have been previously demonstrated to reduce the psychological burden of treatment (5), could be a main contributing factor to the positive association observed between use and clinical outcomes. A recent RCT showed that information alone could significantly increase satisfaction and knowledge, but clinical outcomes were not investigated (17). The higher use of medication management than the emotional component also suggests that medication adherence could be an additional explanation. A systematic review noted widely varying rates of adherence in fertility care (range, 28%–81%), lending support to this possibility, but none of the studies examined adherence in stimulated cycles (18). Whether the association is because of use overall, or use of the specific components of the application, should be, as noted, an area for future explorative research, but both could be contributing. The focus in this paper is MediEmo, but other digital resources having similar features should also be investigated.

Despite an association with higher LBR on the fresh index cycle and higher return rates, descriptive statistics showed that the difference between users and nonusers for the complete cycle LBR was not significant (41% users vs. 35% nonusers), although the association was in the expected direction. An association between multiple complete cycles and higher cumulative pregnancy rate is expected and well established (19). Given the effect size, we were underpowered but other factors could explain the lack of effect on the complete cycle not captured in the present study (e.g., underlying differences

in embryo quality in thaw cycles). Future research should be inclusive of variables hypothesized in the path to impact on clinical outcomes to fully capture benefits of digital tools such as MediEmo, for example, reduction of burden via impacts on stress hormones (20) or via behavioral mechanisms (e.g., predictors of return rates) (21). Additionally, were the association between MediEmo use and clinical outcomes confirmed, it would be worthwhile to determine when and how such tools could be introduced to patients. Recent research suggests that IVF practice should pivot toward multicycle planning vs. current norms of single cycle planning (22–24) and availability of digital apps such as MediEmo that are associated with return rates could bolster willingness to engage with this normative change.

Increasing patient and staff interest and engagement with MediEmo, particularly the emotional tracking, is key to maximizing the reach and functionality of this and other digital support applications. As we discussed previously, engagement with the emotional component (>60%) was higher than typically reported for in-person support (4). Iterative improvement, with responsiveness to patient feedback and coproduction of any new features is likely to increase this utility. For example, a problem identified with MediEmo in our previous work was that patients who entered emotional scores representing distress felt not enough was done with this information ("Whilst I liked logging my mood each day there was no feedback or any further discussion over this or the results", Robertson et al. 2022 (4), Supplemental Materials and Methods, p. 3). It is imperative that algorithms are optimized to ensure that when patients record struggling with the emotional impact of their IVF cycle, this signal is acted on by the clinic so that health care professionals can provide support in a timely manner. The MediEmo application has an algorithm to trigger patient support, but future research needs to ensure thresholds are set to levels at which patients feel supported. This is a challenge that concerns eliciting patient preferences, selecting the best variables for optimization/personalization, and dealing with implementation factors enabled with artificial intelligence and machine learning (25). Using the MediEmo to improve communication between patients and staff is one of the current developments in progress for the app.

Strengths and limitations

There are several limitations to this study. Because of its observational nature, we can only describe the association between the MediEmo application and recorded variables at a single institution and are unable to imply causation of the observed difference between users and nonusers. Efficacy testing will be a critical next step in establishing whether the MediEmo results in a causal change in behavior and reproductive clinical outcomes. A multicentre RCT of the effect of MediEmo on treatment return and LBRs would be beneficial, but such an RCT would need to recruit a large sample and have a prolonged period of follow up to reliably assess live birth, return rates after a failed complete cycle of treatment (i.e., minimum, 12 months per patient) and LBR per complete cycle. There is also a need for randomization to control for the many potential confounders we have highlighted in the discussion (26). Although our controlled analysis suggested the confounder age was not likely to be a principal cause of associations with live birth and return rates, we acknowledge that more confounders (e.g., socioeconomic status, ethnicity, infertility duration, previous births, BMI, and previous miscarriages) should be included in future research. Usage statistics reported elsewhere (4) demonstrated that nonapplication use was more likely because of accessibility issues as mentioned. In this study, we also saw that people with social infertility were less likely to use the MediEmo application. Such results are important when considering the associations found and whether they are the result of application usage or individual characteristics. As suggested previously, the associations found may be because of sample bias. For example, patients who use mobile applications may be more motivated to engage and comply with treatment and more financially able and likely to return for treatment after experiencing an unsuccessful cycle. Similarly, patients who perceive themselves to have a better treatment prognosis may be more likely to return for treatment after an unsuccessful cycle. Future research should therefore consider the impact of patient sociodemographics and measure treatment motivation and perceptions of treatment success. Again, this highlights the importance of undertaking an RCT and not relying solely on formative studies especially that RCTs of digital health interventions have been shown to at times overturn conclusions made from observational or nonrandomized studies (27). A definitive RCT trial can only be undertaken once and is best performed only when the digital tool is relatively stable, can be implemented with high fidelity and the overall benefits expected to be clinically meaningful (28). Cost benefits of implementation could also be examined in such trials as recent evidence suggests high return rates for cognitive-type interventions such as MediEmo (29). The development and early evaluation phase of the MediEmo application has demonstrated good user experiences, relevant association with proposed outcomes, suggesting it can be moved to the next stages of evaluation.

CONCLUSION

Digital tools, including applications, are increasingly used alongside fertility and other medical treatments. Our study on MediEmo use demonstrates that if application development draws on existing research evidence and focuses on patient and staff needs and preferences, it is possible to develop a practical, easily scalable tool, leading to high uptake and the possibility of measurable benefit to patients.

CRediT Authorship Contribution Statement

Isla F. China R. Robertson Harrison: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Richard D. Morey:** Writing – review & editing, Writing – original draft. **Jacky Boivin:** Writing – review & editing, Formal analysis. **Ying Cheong:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of Interests

Outside of the submitted work, J.B. reports personal speaker fees from Merck Group, Organon, Ferring, consultancy fees outside the submitted work from Ferring Pharmaceuticals A/S, that she is co-developer of the MediEmo application and that J.B.'s employer Cardiff University owns one third of shares in MediEmo. Y.C. reports personal speaker fees from Merck, Ferring Pharmaceuticals, Organon and is a minority shareholder in the MediEmo app. None of the shareholders have benefited financially from MediEmo. I.F.R., C.R.H., and R.D.M. declare no conflicts of interest.

Data availability

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

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be found online at https://doi.org/10.1016/j.xfre.2025.04.003.

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