The EMPOWER blended digital intervention for relapse prevention in schizophrenia: a feasibility cluster randomised controlled trial in Scotland and Australia

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Summary

Background Early warning signs monitoring by service users with schizophrenia has shown promise in preventing relapse but the quality of evidence is low. We aimed to establish the feasibility of undertaking a definitive randomised controlled trial to determine the effectiveness of a blended digital intervention for relapse prevention in schizophrenia.

Methods This multicentre, feasibility, cluster randomised controlled trial aimed to compare Early signs Monitoring to Prevent relapse in psychosis and prOmote Well-being, Engagement, and Recovery (EMPOWER) with treatment as usual in community mental health services (CMHS) in Glasgow and Melbourne. CMHS were the unit of randomisation, selected on the basis of those that probably had five or more care coordinators willing to participate. Participants were eligible if they were older than 16 years, had a schizophrenia or related diagnosis confirmed via case records, were able to provide informed consent, had contact with CMHS, and had had a relapse within the previous 2 years. Participants were randomised within stratified clusters to EMPOWER or to continue their usual approach to care. EMPOWER blended a smartphone for active monitoring of early warning signs with peer support to promote self-management and clinical triage to promote access to relapse prevention. Main outcomes were feasibility, acceptability, usability, and safety, which was assessed through face-to-face interviews. App usage was assessed via the smartphone and self-report. Primary end point was 12 months. Participants, research assistants and other team members involved in delivering the intervention were not masked to treatment conditions. Assessment of relapse was done by an independent adjudication panel masked to randomisation group. The study is registered at ISRCTN (99559262).

Findings We identified and randomised eight CMHS (six in Glasgow and two in Melbourne) comprising 47 care coordinators. We recruited 86 service users between Jan 19 and Aug 8, 2018; 73 were randomised (42 [58%] to EMPOWER and 31 [42%] to treatment as usual). There were 37 (51%) men and 36 (49%) women. At 12 months, main outcomes were collected for 32 (76%) of service users in the EMPOWER group and 30 (97%) of service users in the treatment as usual group. Of those randomised to EMPOWER, 30 (71%) met our a priori criterion of more than 33% adherence to daily monitoring that assumed feasibility. Median time to discontinuation of these participants was 31·5 weeks (SD 14·5). There were 29 adverse events in the EMPOWER group and 25 adverse events in the treatment as usual group. There were 13 app-related adverse events, affecting 11 people, one of which was serious. Fear of relapse was lower in the EMPOWER group than in the treatment as usual group at 12 months (mean difference –7·53 (95% CI –14·45 to 0·60; Cohen's *d* –0·53).

Interpretation A trial of digital technology to monitor early warning signs blended with peer support and clinical triage to detect and prevent relapse appears to be feasible, safe, and acceptable. A further main trial is merited.

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Introduction

Schizophrenia contributes substantially to global burden of disease[1] and follows a recurring course; the relapse rate is 80% within 5-years of follow-up.[2] Relapses threaten long-term recovery and contribute considerably to treatment costs.[3,4] The distress of relapse and risk of traumatisation associated with rehospitalisations warrant attention to relapse prevention in schizophrenia treatment guidelines.[5]

Birchwood and colleagues pioneered the involvement of individuals and carers in monitoring early warning signs of relapse to enable timely biopsychosocial interventions.[6] However, there are outstanding questions regarding the effectiveness of this approach. The quality

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Research in context

Evidence before this study

We searched Web of Science, MEDLINE, and PubMed for English language systematic reviews and meta-analyses published between Jan 1, 2000, and Feb 15, 2021, that reported on the effectiveness of relapse prevention interventions based upon the detection of early warnings signs of relapse reported by people diagnosed with schizophrenia. We used the search terms "relapse prevention", "early warning signs", and "schizophrenia". We also checked citation reports for updated evidence.
A Cochrane review (2013) focused on the effectiveness of interventions targeting recognition and management of early warning signs of relapse in schizophrenia. Significant effects in favour of early warning signs interventions plus treatment as usual compared with treatment as usual alone were found for the proportion of participants relapsing and the number of participants being rehospitalised. However, neither time to relapse nor time to rehospitalisation differed between the groups. The methodological quality of the trials was poor in terms of randomisation, concealment, and blinding. There is recent evidence for the increasing use and acceptability of mobile smartphone technology by people diagnosed with schizophrenia, for early warning signs for up to 6 months duration. However, it remains unclear if relapse prevention using mobile smartphone technology is acceptable to service users over longer durations than 6 months or if these platforms are effective in preventing psychotic relapse over and above existing treatments.

Added value of this study

The EMPOWER study, done over two countries, provided important feasibility and acceptability data on the use over 12 months of smartphone technology for the prevention of psychotic relapse. Our findings were the first to show that service users identified as being at elevated risk for relapse in schizophrenia can be successfully and safely engaged with a smartphone app entailing both self-monitoring capabilities and an intervention delivered in real-time combined with peer support for relapse prevention for up to 12 months (mean usage 31·5 weeks). We found a high rate of adherence to monitoring with 71% of randomly assigned participants exceeding our a priori measure of acceptable engagement of 33% daily usage. Our findings also indicate important safety considerations for trials of interventions focused on the use of early warning signs for the detection and prevention of relapse in schizophrenia.

Implications of all the available evidence

Early warning signs interventions might reduce the risk of psychotic relapse. The use of smartphone technologies is a promising innovation in the delivery of these interventions. Our findings suggest that smartphone technology combined with clinical triage and peer support can successfully and safely engage service users who are identified as being at elevated risk for schizophrenia in self-monitoring for early warning signs. A future full-scale randomised controlled trial is required to ascertain definitive support for the effectiveness of the EMPOWER intervention. Ascertaining the specific contributions to effectiveness from clinical triage, peer support, and smartphone components in the prevention of relapse is also a priority for further research.

of evidence from randomised controlled trials evaluating the effectiveness of early warning signs monitoring has been assessed as low.[7,8] People's experience of relapse and its management leads to specific fear of its recurrence.[9] A potential solution is an early warning signs framework to support people's need for safety and self-efficacy. Smartphone technology, by facilitating control over real-time personal data, has potential to foster awareness of symptoms and associated experiences over time.[10] Furthermore, a human presence supporting self-efficacy and autonomy is important for active engagement in digital health interventions.[11] Therefore, in the context of recurring psychosis and lingering fear of relapse, digital interventions, blended with peer support to promote self-management and clinical triage enabling timely human support and shared decision making, offer an important opportunity for relapse prevention. However, no previous relapse prevention intervention for schizophrenia has integrated all these components.[12]

The aim of the current study was to establish the feasibility of a definitive randomised controlled trial to determine the effectiveness of the Early signs Monitoring to Prevent relapse in psychosis and prOmote Well-being, Engagement, and Recovery (EMPOWER) early warning signs intervention, which supports self-efficacy by integrating a smartphone early warning signs app with peer support for people diagnosed with schizophrenia at high risk of relapse. Given that we sought to embed smartphone monitoring with clinical triage into existing community-based relapse prevention care pathways, we chose a cluster design to compare EMPOWER with treatment as usual in community mental health services in Scotland and Australia. The objectives of the trial pertained to both the cluster and individual level.

Methods

Study design

This multicentre, two parallel grouped, feasibility cluster randomised controlled trial of the EMPOWER intervention with 12-month follow-up was completed in 8 purposively selected community mental health services (CMHS); two in Melbourne, Australia and six in Glasgow, UK. The study received ethical approval from West of Scotland Research Ethics Service (16/WS/0225) and

Melbourne Health Human Research Ethics Committee (HREC/15/MH/344). The study also received a notice of no objection for the trial of a class 1 medical device (CI/2017/0039) from the UK Medicines and Healthcare products Regulatory Agency (MHRA). The study was planned and implemented in concordance with the Consolidated Standards of Reporting Trials (CONSORT) cluster trial extension,[13] and we separately published a study protocol.[14] A cluster design was chosen because the EMPOWER intervention aimed to facilitate access to team-based relapse prevention care pathways by providing real-time early warning signs monitoring data.

Participants

We identified CMHS likely to have five or more care coordinators willing to participate with eligible service users on their caseload (before the recruitment of CMHS investigators, AG, SB, and JF met with staff at potential sites to ascertain their eligibility and willingness to participate in the study). Researchers approached care coordinators and sought their consent to participate. Before randomisation, consenting care coordinators provided researcher workers with an anonymised list of potentially eligible service users on their caseload. Care coordinators provided participants with an information leaflet about the study to facilitate the expression of interest to participate.

Service users were eligible if they were older than 16 years, had a schizophrenia or related diagnosis confirmed via case records (ICD10 F20·81, F25, F20·9, or F22), and were able to provide informed consent, as determined by the care coordinator or responsible consultant. Patients also had to be on the current caseload of participating CMHS, to have had contact with CMHS, and to have experienced a relapse within the previous 2 years. For eligibility purposes, we defined relapse of psychosis as either a psychiatric inpatient admission at least once in the previous 2 years or having received crisis intervention in the previous 2 years. Eligible patients who had recently been discharged to CMHS from inpatient or crisis services were not contacted for informed consent within 4 weeks of that transfer of care. Carers of people receiving support from participating services were eligible for inclusion if nominated by an eligible participant and were in regular contact with that participant. We measured carers' exploratory clinical outcomes and resource use, which will be reported elsewhere. All participants were approached for informed and written consent before assessment and randomisation by trained research assistants.

Randomisation and masking

Participating CMHS were randomised within stratified pairs (the clusters) to the EMPOWER relapse prevention intervention or to continue their usual approach to care. After the completion of baseline assessments, randomisation of the CMHS was completed by the Centre for Healthcare Randomised Trials (CHaRT). CMHS were randomised within stratified pairs. A statistician at the CHaRT provided the allocation codes. The two clusters in Australia formed a single stratum. The six clusters in Glasgow were paired based on similarity of catchment area in terms of social deprivation or CMHS type (eg, early intervention service). Research assistants and other team members involved in delivering the intervention were not masked to treatment condition but our assessment of relapse was masked. The trial statistician was also masked to the relapse outcome until the final data cut. More detail on randomisation and masking can be found in the protocol paper.[14]

Procedures

The EMPOWER intervention, described in detail elsewhere[14] and in the appendix (pp 1–16), blended peer and clinician support with a smartphone app that allowed people using it to monitor their wellbeing and possible early warning signs of schizophrenia relapse. The rationale for the intervention, which was available for up to 12 months, was informed by our cognitive interpersonal model.[14] The EMPOWER software was built using the ClinTouch (version 3.0) software platform.[15]

See Online for appendix

Daily phone notifications prompted app users to respond to a core 22-item questionnaire with additional items seeking further detail dependent on initial rating. Following questionnaire completion, app users received messages designed to enhance self-management and autonomy and that were tailored to questionnaire responses. The messages included in the app were informed by consultation with people with lived experience of psychosis. The app allowed users to view the ebb and flow of changes in wellbeing via charts of their self-ratings. The analysis of data submitted through the app was governed by an algorithm, which was a class 1 medical device (CI/2017/0039 [University of Manchester, Manchester, UK]). This analysis formed one part of a broader system designed to identify and respond to changes in wellbeing that were suggestive of early warning signs.

Following a 4-week monitoring period establishing a personal baseline for app users, the algorithm initiated the comparison of a participant's latest data against baseline. If changes exceeded predefined thresholds, a check-in prompt was generated for that participant and AG and EM were made aware of it via email. Clinical staff, who included a registered mental health nurse (UK only), clinical psychologists (UK and Australia), and a general psychologist (Australia only), also used a web interface to review data to inform their judgement on how best to respond to a check-in prompt. We aimed to respond to check-in prompts within 24 h or by the next working day. If, for any reason, participants were unable to complete a 4-week monitoring period (eg, because of relapse or another stressful life event), they were given

the opportunity to restart baseline monitoring as soon as the relevant event was resolved.

Peer support workers were employed in the UK and Australia to work with people in the intervention group. Their roles included supporting setup and engagement with the app, offering technical advice and support, and monitoring performance and safety issues. The peer support workers encouraged people to reflect on their experiences of monitoring wellbeing and, as appropriate, they provided information on wellbeing resources and sources of support. Peer support workers' contact with participants was roughly fortnightly and was most commonly via telephone.

Treatment as usual was chosen as a control condition as this provided a fair comparison with routine clinical practice. In Glasgow and Melbourne, treatment as usual was secondary care and relapse prevention delivered by adult community services, which largely involved regular follow-up with a care coordinator and periodic review by a psychiatrist.

In addition to the routine collection of app-based data for those in the intervention group, researcher assessments were completed at baseline, 3 months, 6 months, and 12 months for all participants. Mental health status was measured with the Positive and Negative Syndrome Scale (PANSS), Personal and Social Performance Scale, and the Calgary Depression Scale for Schizophrenia. Emotional distress was assessed with the Hospital Anxiety and Depression Scale and the Personal Beliefs About Illness Questionnaire-Revised (PBIQ-R). Substance misuse was assessed with the Timeline Followback for drugs and alcohol (over 28 days; appendix p 34). Research assistants who were not masked to treatment group assessed participants using observational and self report measures either in the participant's home or their local CMHS. These were completed by trained research assistants who underwent regular inter-rater reliability monitoring during the trial. All research assistants completed a structured training programme to calibrate their performance to observational measures. Feedback on ratings was anchored to a set of training recordings and videos, with reference ratings provided by an expert rater and then checked for consensus agreement with at least 3 other raters until consistency was achieved. Raters subsequently met on a monthly basis for reliability assessment. If a rater showed a deviation of greater than 2 points on any item, they received feedback and additional supervision. Nine separate observational assessments were audio recorded and rated during the study period.

Research assistants who were independent of the experimental treatment systematically screened electronic case records and extracted data according to a structured protocol (appendix pp 17–33). Research assistants started from the most recent clinical entry and worked back through the preceding clinical entries for the specified time period and identified changes in clinical response and management, symptoms, risk, and functioning that might have been indicative of relapse according to the criteria. All information regarding EMPOWER was masked and any identifiable information regarding the participant was removed. Compliance with the protocol was supervised by AG. Following this assessment, anonymised vignettes were passed by SB, the trial manager, using encrypted file sharing for review by our independent adjudication panel, which comprised experienced clinician researchers (Matthias Schwannauer and Sandra Bucci). Inter-rater reliability based on a sample of 12 assessments was high (k=0·80).

Outcomes

Our main outcomes were establishing feasibility, acceptability, usability, and safety, which were assessed in the intention-to-treat population which included all participants from each randomised cluster. We also included several exploratory clinical outcomes to aid in designing and planning a future definitive clinical trial (appendix pp 40–41).

Feasibility was a priori operationalised as proportion of eligible service users who consented to enter the study, remained in the study, and provided relapse outcomes data. To measure usability in participants from CMHS randomised to EMPOWER, we assessed duration of app usage per participant and the number of participants completing more than 33% of early warning signs questionnaires. Previous digital research in schizophrenia has used an ecological monetary assessment response rate of 33% for data to be considered reliable[16,17] and this cutoff has been used in a recent study of early warning signs and relapse utilising the ClinTouch platform.[18] We assessed app usability on the basis of participants' daily completion of the app questionnaire recorded on the ClinTouch platform. We calculated app usability from the start of baseline monitoring until 4 consecutive weeks of app usage falling below 33%. In addition, we measured, using a purposely designed questionnaire for use in this study, self-reported frequency of app usage (on the 5 point scale in which 5 represents daily use), sharing data from the app with others (on a scale of 4, in which 1 is not at all and 4 is often), and the use of charts. Acceptability was assessed with an adapted version of the Mobile Application Rating Scale user version (uMARS), which is a reliable method to assess the reliability of the quality of mobile health apps. uMARS was adapted to ensure items corresponded to relevant features of the EMPOWER app.[19] Safety was measured, in line with medical devices regulations 2002,[20] associated guidance provided in MEDDEV 2.1/6, and ISO/FDIS 14155:2011, as all untoward medical occurrences or clinical indications, their relatedness to the investigational medical device and to wider study procedures, their seriousness and intensity, and whether the event was anticipated. We have previously argued that, given the lack of specificity of early signs to relapse, early warning signs monitoring might unduly increase

	EMPOWER (n=42)	TAU (n=31)
Gender		
Men	21 (50%)	16 (52)
Women	21 (50%)	15 (48)
Other	0	0
Age, years	42 (13)	43 (12)
Years of education	12 (3)*	13 (3)†
First contact with mental health services, months	154 (121)‡	134 (92)†
Participant identified a carer	10 (24%)	17 (55%)
Ethnicity and birthplace		
UK participants	30 (71%)	19 (61%)
Scottish ethnicity	21/30 (70%)	16/19 (84%)
Other British ethnicity	1/30 (3%)	1/19 (5%)
Other White ethnicity	1/30 (3%)	0
Mixed ethnicity	1/30 (3%)	1/19 (5%)
Pakistani ethnicity	2/30 (7%)	0
Indian ethnicity	1/30 (3%)	0
African ethnicity	3/30 (10%)	0
Unknown ethnicity	0	1/19 (5%)
Australian participants	12 (29%)	12 (39%)
Born in Australia	7/12 (58%)	12/12 (100%)
Born elsewhere	5/12 (42%)	0
Aboriginal/Torres Strait ethnicity	0	1/12 (8%)
Remission at baseline		
Full remission	20 (48%)	12 (39%)
Partial remission	19 (45%)	18 (58%)
Inadequate evidence	2 (5%)	1 (3%)
Missing data	1 (2%)	0
Positive and Negative Syndrome Scale		
Positive	14·83 (5·92)	15·43 (6·68)†
Negative	13·90 (5·45)	12·47 (4·08)†
Disorganisation	15·86 (7·17)	14·63 (4·67)†
Excitement	4·95 (1·65)	4·33 (0·55)†
Emotional distress	11·95 (4·40)	12·07 (3·24)†
Total	61·50 (18·14)	58·93 (13·73)†
Personal and Social Performance Scale	56·86 (16·02)	59·37 (19·29)†
Calgary Depression Schizophrenia Scale	6·93 (5·34)	6·97 (4·15)†
Alcohol used in the past 28 days		
Used	15 (36%)	12 (39%)
Not used	26 (62%)	18 (58%)
Missing	1 (2%)	1 (3%)
Cannabis used in the past 28 days		
Used	7 (17%)	5 (16%)
Not used	34 (81%)	25 (81%)
Missing	1 (2%)	1 (3%)
Other main drug used in the past 28 days		
Used	4 (10%)	5 (16%)
Not used	37 (88%)	25 (81%)
Missing	1 (2%)	1 (3%)
Hospital Anxiety Depression Scale		
Anxiety	9·76 (5·11)†	10·70 (4·88)†
Depression	7·38 (4·98)§	8·03 (4·66)§
Personal Beliefs about Illness Questionnaire		
Control	10·29 (2·52)†	9·83 (2·61)†
Shame	10·10 (2·96)†	10·67 (3·07)†
Entrapment	10·73 (2·88)†	10·80 (3·38)†
Loss	9·84 (2·82)†	10·20 (2·54)†
Socially marginalised	11·64 (2·89)†	11·87 (2·75)†

(Table 1 continues in next column)

(Continued from previous column)

Data are n (%) or mean (SD). *Data are missing for seven participants. †Data are missing for one participant. ‡Data are missing for four participants. §Data are missing for two participants.

Table 1: **Baseline demographics and clinical characteristics**

fear of relapse. We therefore assessed fear of relapse using the Fear of Recurrence Scale.[9] We also measured several performance endpoints, with more details found in the appendix (p 39).

Choice of measures

Our primary aim was to establish the feasibility of undertaking a definitive randomised controlled trial to determine the effectiveness of EMPOWER versus treatment as usual in preventing relapse in people with schizophrenia. In order to determine this we measured multiple parameters including the proportion of eligible service users who consented to enter the study, remained in the study, and provided relapse outcomes data, and the usability, acceptability, and safety of the EMPOWER intervention. We selected the uMARS as a reliable measure of the acceptability of mobile apps. To assess safety we measured adverse events and we used the Fear of Recurrence Scale (FoRSe) to measure if daily early warning signs monitoring increased fear of relapse.

Statistical analysis

A statistical analysis plan was published before the analysis.[21] The target sample size was eight clusters each recruiting 15 participants, for a total of 120 participants. As this is a feasibility study, the sample size was not based on a formal calculation but on logistical and practical considerations, and recommendations from Teare and colleagues.[22] All analyses used the intention-to-treat principle with data from all participants included. Both groups of the study were described at all timepoints using means (with SDs), medians (with IQRs), and numbers (with percentages), as relevant. The candidate primary outcome of relapse was analysed as a binary variable using a generalised linear model, as a modified random-effects multilevel Poisson regression with a log-link function and robust error variance.[23] Our model was adjusted for a fixed country effect and accounted for possible CMHS

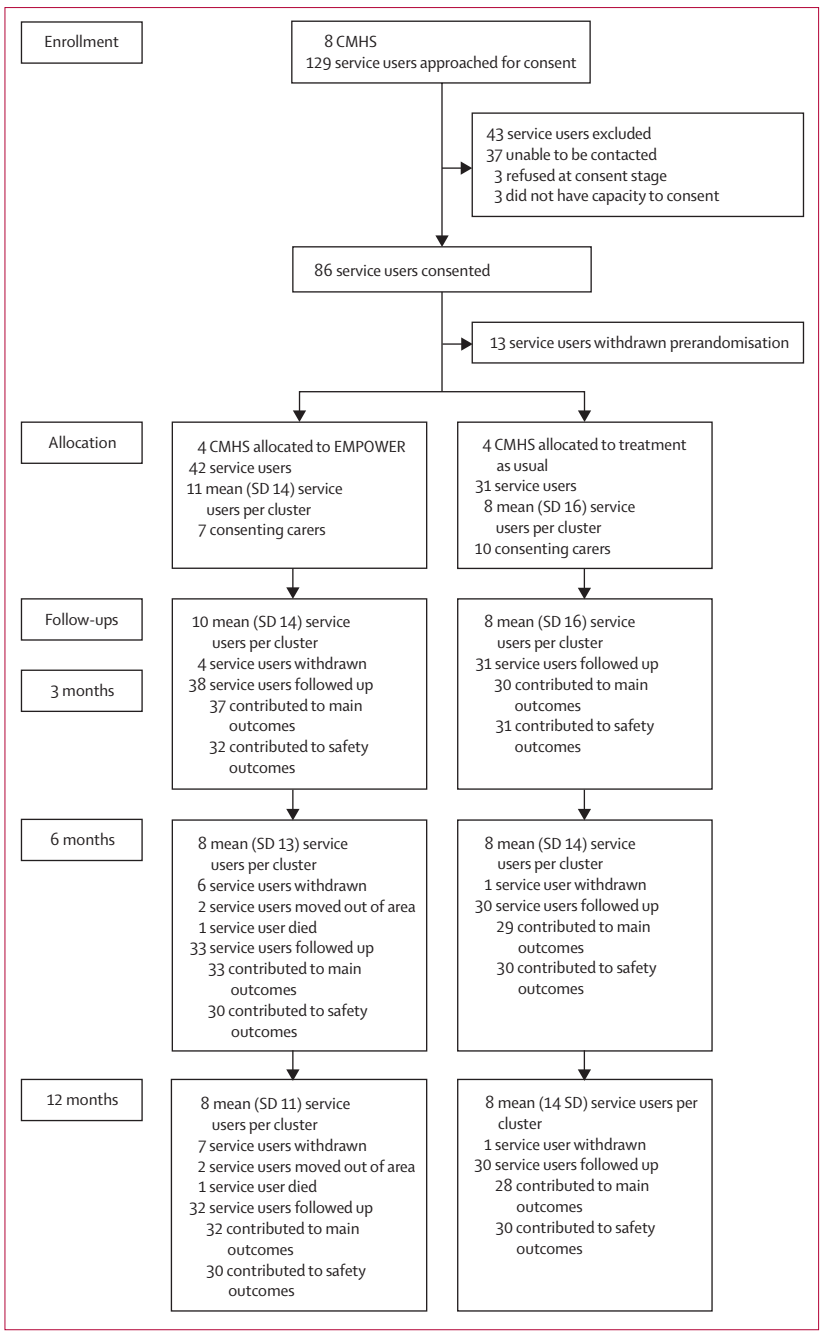

Figure: **CONSORT flow diagram**
CMHS=community mental health services.

clustering. Time to first relapse was assessed using Cox regression. For exploratory clinical outcomes, we used mixed random-effects generalised linear models adjusted for baseline scores, fixed country, and random centre effects. We examined 95% CIs for outcomes and effect sizes using Cohen's *d*.[24] A data monitoring and ethics committee oversaw the study which was preregistered (ISRCTN99559262). Analyses were done using Stata version 15.

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We identified and randomised eight CMHS comprising 47 care coordinators. We contacted 129 of 263 potentially eligible service users between the Jan 19 and Aug 8, 2018, to seek informed consent; 86 (67%) of 129 service users provided informed consent to participate. 13 people withdrew from the study before treatment allocation was revealed leaving 73 participants (37 [51%] men, 36 [49%] women, and no participants identifying as any other gender; 49 [67%] from Scotland and 24 [33%] from Australia. Ethnicity in UK and Australia are presented separately due to local differences in recording (table 1).

17 (63%) of 27 identified carers provided informed consent to participate. Four CMHS were randomised to each group of the study (three CMHS in Glasgow and one CMHS in Melbourne per group). 42 (58%) participants were allocated to the EMPOWER group and 31 (42%) to treatment as usual. During the study, seven people withdrew from the EMPOWER group (including one participant who did not have the app set up), two people moved out of the area, and one person died (the death was not study-related). One person from the treatment as usual group withdrew (figure). Baseline clinical measures showed moderate levels of psychosis, high levels of depression, and marked impairment of functioning (table 1). Low levels of alcohol and drug use were observed at baseline (table 1). Baseline characteristics of carers and care coordinators are summarised in the appendix (p 36). At 12 months, relapse outcomes were collected for 32 (76%) of 42 service users in the EMPOWER group and 30 (97%) of 31 service users in the treatment as usual group (appendix p 38).

In terms of actual app use, of the 41 participants who had the app set up, 33 (81%) completed the 4-week baseline monitoring period. These participants used the app for a mean of 31·5 weeks (SD 14·5; range 6–50). During that period, participants used the app for an average of 4·5 (64%) of 7 days a week (SD 22·5; range 76·3 [20·6–96·9]).

According to our a priori criterion of acceptable engagement of 33% daily usage, 30 participants (91% of the 33 who met the baseline requirement for app use) met our criterion for adherence at 12 months. Of the 42 randomised to EMPOWER, these 30 participants represent 71% who met the criterion. This range of 71% to 91% provides a broader estimate of overall engagement. Over the three follow-up periods, the range of mean self-reported app usage was 4·63–4·65 (table 2). Over the three follow-up periods, mean self-reported sharing of data with keyworkers and family members was 2·04–2·45. The mean ratings of sharing with carers over the three follow up periods was 1·71–1·96. This indicates

that although individuals reported using the app regularly, they were less likely to share these data with staff and family members. Acceptability ratings on the uMARs scale suggested that the app was interesting to use (ranging from 3·52–3·93 over the three follow-ups), easy to learn (4·12–4·17), the content was well written (4·04–4·13), and the content was credible (4·45–4·57). The overall rating for the app was positive (ranging from 4·06–4·31 over the three follow-up periods). There were indications of mental health benefits in this group, with positive ratings for increasing awareness (3·97–4·46), knowledge (3·76–4·19), attitudes (3·72–4·04), motivation (3·87–4·35) and encouragement towards help seeking (4·09–4·14). Performance endpoints as specified at the outset of the trial were met. Check-in prompts are reported in the appendix (p 4).

There were 29 adverse events affecting 19 participants in the EMPOWER group, with 11 events classified as serious adverse events, and 25 adverse events affecting ten people in the treatment as usual group with 15 events classified as serious adverse events (table 3). There were no adverse events related to the EMPOWER class 1 medical device. To ensure a complete picture of adverse events, we monitored for adverse responses to any aspect of the app, identifying 13 app-related adverse events that affected 11 people, one of which was serious —a hospital admission in part related to feeling overwhelmed at the point of app installation. Fear of relapse was lower in the EMPOWER group than in the treatment as usual group at 12 months (mean difference –7·53 (95% CI –14·45 to 0·60, Cohen's *d* –0·53), suggesting routine monitoring did not exacerbate hypervigilance or anxiety about illness (appendix p 37). Adverse events are described in more detail in a previous publication.[25] Exploratory clinical outcomes can be found in the appendix (pp 40–41).

	3 months (n=38)	6 months (n=33)	12 months (n=32)
App usage			
Roughly how often participants used app*	30: 4·63 (0·96)	26: 4·65 (0·75)	23: 4·65 (0·57)
Not at all	1/33 (3%)	0	0
Roughly how often participants shared the app with keyworker†	26: 2·04 (1·00)	25: 2·24 (1·16)	22: 2·45 (1·30)
Not sure	3/29 (10%)	1/26 (4)	1/23 (4%)
Roughly how often participants shared app with family†	28: 1·71 (0·98)	26: 1·96 (1·15)	22: 1·91 (1·19)
Not sure	1/29 (3%)	0	1/23 (4%)
Roughly how often participants accessed charts‡	28: 3·04 (0·74)	26: 2·54 (1·14)	23: 3·00 (1·04)
Not sure	1/29 (3%)	0	0
uMARS‡			
Is the app interesting to use?	29: 3·93 (0·88)	26: 3·92 (0·98)	23: 3·52 (0·99)
How easy is it to learn how to use the app; how clear are the menu labels, icons and instructions?	29: 4·14 (0·64)	26: 4·12 (0·91)	23: 4·17 (0·78)
Moving or links between screens work?	29: 3·97 (0·87)	26: 4·12 (0·71)	23: 4·17 (0·78)
Is app content correct, well written, and relevant?	29: 4·07 (0·70)	26: 4·04 (0·77)	23: 4·13 (0·69)
Is app information from a credible source?	29: 4·45 (0·78)	26: 4·58 (0·58)	23: 4·57 (0·66)
Would you recommend the EMPOWER app?	29: 3·83 (1·07)	26: 3·85 (1·12)	23: 3·83 (1·34)
How do you rate the app?	19: 4·26 (0·81)	16: 4·31 (0·79)	17: 4·06 (0·75)
NA	10 (33)	10 (38)	6 (26)
App has increased awareness	29: 3·97 (0·98)	26: 4·46 (0·71)	23: 4·22 (1·04)
App has increased knowledge or understanding	29: 3·76 (1·09)	26: 4·19 (0·80)	23: 3·96 (1·02)
App changed attitudes toward improvement	29: 3·72 (0·88)	26: 4·04 (0·96)	23: 3·83 (1·03)
App increased my intentions and motivation	29: 3·97 (0·87)	26: 4·35 (0·75)	23: 3·87 (0·97)
App encourages me to seek help	29: 4·14 (0·88)	26: 4·42 (0·70)	23: 4·09 (1·04)

Data are n (%) and n: mean (SD). Numbers of participants completing each item do not equal column totals due to missing data. uMARS=Mobile Application Rating Scale user version. NA=not answered. *Scale of 1 to 5 (since last assessment) in which 1 is not at all, 2 is once a month, 3 is a few times a month, 4 is weekly, and 5 is daily. †Scale of 1 to 4 (since last assessment) in which 1 is not at all, 2 is rarely, 3 is sometimes, and 4 is often. ‡Questions are answered on a scale of 1 to 5, with higher scores indicating better app acceptability and lower scores worse app acceptability.

Table 2: **Acceptability and usability of the EMPOWER app**

Discussion

We established the feasibility of a definitive randomised controlled trial and tested acceptability, usability, and safety of the EMPOWER intervention. We recruited and retained clinical services, screened caseloads, and gained informed consent to participate from 86 patients (of whom we randomly assigned 73). Rates of overall follow-up were good over the 12 months, with data availability between 73% and 85%. We also successfully gathered consent and recruited 47 care coordinators to the study. We noted during the study high rates of turnover amongst coordinators and this was reflected in lower rates of data availability at 12 months (31 [42%] of 73). Service user participants identified 27 carers, of whom 17 (63%) gave their consent to participate (seven [70%] of ten carers from the EMPOWER group and ten (59%) of 17 carers from the treatment as usual group). Taken together, these results provide support for the feasibility, recruitment, and follow-up of service user participants in a future trial.

We found high rates of engagement with the app: 91% of users (71% of those randomised) exceeded our a priori threshold for adherence (33%). People used the app for a mean of 31·5 weeks. Participants self-reported using the app on a weekly to daily basis during follow-up. There were good levels of acceptability and usability. However, participants reported only moderate willingness to share their data with keyworkers and carers. Contact with research staff providing clinical triage of check-in prompts and peer support probably contributed to the high levels of app engagement that we observed, in line with wider evidence for the role of human support for digital interventions for psychosis.[26] Blending of interventions might be an important means of addressing service user concerns that digital tools should not be a replacement for face-to-face contact.[27,28]

We identified important safety signals related to the EMPOWER intervention. However, we detected 13 app-related adverse events, one serious (appendix p 38). These findings need to be addressed in future iterations of EMPOWER. Our findings raise important concerns

	EMPOWER (n=42)	Treatment as usual (n=31)
Number of participants with an adverse event	19 (45%)	10 (32%)
Men	8/19 (42%)	4/10 (40%)
Women	11/19 (58%)	6/10 (60%)
Number of adverse events	29	25
Number of serious adverse events	11/29 (38%)	15/25 (60%)
Number of anticipated serious adverse events	7/11 (64%)	14/15 (93%)
Number of serious adverse events resulting in death	1/11 (9%)	0
Serious adverse event relatedness		
Number of serious adverse events related to study procedure*	1/11 (9%)	0
Number of serious adverse events related the app	1/11 (9%)	0
Number of serious adverse events related to the medical device	0	0
Adverse event relatedness†		
Number of adverse events related to study procedure*	3/18 (17%)	2/10 (20%)
Number of adverse events related the app	12/18 (67%)	0
Number of adverse events related to the medical device	0	0
Intensity of serious adverse events		
Mild	1/11 (9%)	0
Moderate	1/11 (9%)	0
Severe	9/11 (82%)	15 (100%)
Intensity of adverse events†		
Mild	3/18 (17%)	4/10 (40%)
Moderate	12/18 (67%)	3/10 (30%)
Severe	3/18 (17%)	3/10 (30%)
Fear of recurrence‡		
Baseline	42: 55·81 (12·89)	30: 52·45 (15·69)
3 months	32: 48·69 (11·05)	28: 53·40 (16·42)
6 months	30: 51·57 (10·49)	25: 50·70 (18·78)
12 months	30: 47·51 (12·90)	28: 52·77 (16·09)

Data are n (%) or n: mean (SD). *Research assessments, for example, but not related to the use of the app. †Not including serious adverse events. ‡Based on the Fear of Recurrence Scale.

Table 3: **Adverse events and fear of relapse**

about wider adverse event monitoring and reporting in digital interventions for psychosis.[25] Enhanced adverse event monitoring allowed us to respond to service user needs and provided essential information about the refinement of the intervention for future research. Future research should adopt rigorous frameworks for safety monitoring and reporting. The trial also included findings for several exploratory clinical outcomes (see appendix pp 40–41) that should be further explored in a fully powered clinical trial.

Previous studies using digital technologies to monitor early warning signs to prevent relapse[18,29] theorised that monitoring for changes in wellbeing would trigger changes in clinician behaviour as a pathway to relapse prevention. In these studies, monitoring was feasible but realising clinician behaviour change was challenging. We found a very high rate of staff turnover and low levels of service user-initiated data sharing. Our theory that EMPOWER would lead to improved shared decision making with clinicians was not supported. The EMPOWER intervention differed from previous studies by the inclusion of three components: self-management messaging in response to monitoring, peer support for self-management, and clinical triage to explore context of changes in early warning signs (to trigger a relapse prevention pathway). Taken together, our findings signal early warning signs-based interventions should incorporate a focus on self-management[30,31] and blended human support. A strength of this intervention was the emphasis of blending digital interventions with human contact, which maximised the potential scalability in mental health services, and which was underpinned by encouraging findings regarding actual app use during the study.

In terms of limitations, we saw higher attrition from the EMPOWER group of the study than the treatment as usual group, which appeared to be related to the additional burden and adverse effects of self-monitoring. We believe that increased intensive support and advice at the outset of app usage from peer workers could help reduce attrition in future research. Further limitations were the absence of a quantitative measure of engagement with self-management activities (ie, tasks required to successfully live with and manage the physical, social, and emotional effect of psychosis) because of the intervention and the need to validate the EMPOWER questionnaire used in the app. Early warning signs data relied on active monitoring by participants. Technological developments incorporating passive sensing have shown promise in the detection of relapse and potential to enhance relapse prevention.[32,33] Future research could combine active and passive monitoring to improve the accuracy of detecting increased risk of relapse, with these data delivered automatically in real time to electronic case records.[18] Finally, sample size did not allow for gender-specific analyses.

With reference to the framework for complex interventions,[34] we anticipate a further phase of research to optimise the intervention and its components, and the evaluation of its effectiveness (including cost effectiveness). We believe that it will be possible to refine and improve the intervention, most notably in relation to peer worker practices, as well as functions and technical features of the app. Importantly, intervention developments should closely involve people with experiences of psychosis in the process.

Contributors

AIG is chief investigator who together with JG and JF developed the study protocol alongside the other co-investigators (JA, MA-J, MB, AB, SB, SBu, SMC, PF, RL, SL, GMacL, CM, JN, MS, SPS, SS, AT, CW, and ARY), and with JG and JF had overall responsibility for the management and delivery of the trial. AIG, JF, JG, SB, and EM finalised the study protocol for implementation. SB was the trial manager and is responsible for coordinating the trial. EM was the trial coordinator in Australia and was responsible for coordinating the trial in Melbourne. HMcL, SB, and EM developed and implemented standard operating procedures for participant assessment and data collection. AG, SB, JF, and EM oversaw the design and implementation of the intervention. MM led the development of the app. LA had full access to, and verified, the raw data and led the statistical analysis and modelling. AB, CM, LE,

and NMcM led the health economic evaluation and modelling. AG, JG, JF, SB, and SA drafted the final manuscript. All authors commented on and approved the final version of the manuscript. AG had full access to all data in the study and final responsibility for the decision to submit for publication.

Declaration of interests

AIG reports personal fees from University of Manchester, personal fees from University of Exeter, personal fees from British Association for Behavioural and Cognitive Psychotherapies and other interests with UK National Health Service (NHS) Education for Scotland outside the submitted work. JA, SL, and SB report other interests with CareLoop Health, outside the submitted work. SB reports grants from the Medical Research Council and UK National Institute for Health Research (NIHR) during the conduct of the study. SL reports grants from the UK Medical Research Council (MRC) during the conduct of the study. JA reports grants from MRC, Engineering and Physical Sciences Research Council, Economic and Social Research Council, NIHR, and the US National Institute for Health, and was a Fellow of the Alan Turing Institute during the conduct of the study. AB reports personal fees from Bayer, Merck, Janssen, Novartis, Sword Health, Amgen, and Daiichi Sankyo outside the submitted work. JF reports grants from National Health and Medical Research Council (Australia) during the conduct of the study and other interests with Melbourne Health (NorthWestern Mental Health) outside the submitted work. HMcL reports grants from NIHR Health Technology Assessment (HTA) during the conduct of the study, and grants with Academy of Medical Sciences, Glasgow Children's Hospital Charity, and Scotland's Chief Scientist's Office. CM reports grants from National Health and Medical Research Council (Australia) during the conduct of the study. JN reports grants from the University of Aberdeen and the University of Edinburgh during the conduct of the study and declares membership of the following NIHR boards: Cardio Pulmonary Resusitation decision making committee; HTA commissioning board; HTA commissioning sub-board (expression of interest); HTA funding boards policy group; HTA general board; HTA post-board funding teleconference; NIHR clinical trials unit standing advisory committee; NIHR HTA and Efficacy Mechanism Evaluation editorial board; pre-exposure prophylaxis impact review panel. PF is a member of the HTA mental health prioritisation panel. CW reports grants from NIHR during the conduct of the study and from the Royal College of Psychiatrists, and other interests with Five Areas outside the submitted work. AY reports an NIHR Senior Investigator Grant. JG reports grants from the National Health Medical Research Council. All other authors declare no competing interests.

Data sharing

Individual participant data that underlie the results reported in this Article, after de-identification, and the statistical analysis plan and analytical code, will be made available following publication, on reasonable request, to researchers who provide a methodologically sound proposal. Proposals should be directed to the corresponding author; to gain access, data requestors will need to sign a data access agreement.

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