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A randomized controlled trial of a digital cognitive-behavioral therapy program (COMPASS) for managing depression and anxiety related to living with a long-term physical health condition

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Original Article

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Abstract

Background. To evaluate the clinical efficacy of COMPASS, a therapist-supported digital therapeutic for reducing psychological distress (anxiety/depression) in people living with long-term physical health conditions (LTCs).

Methods. A two-armed randomized-controlled trial recruiting from LTC charities. Participants with anxiety and/or depression symptoms related to their LTC(s) were randomized (concealed allocation via independent administrator) to COMPASS (access to 11 tailored modules plus five thirty-minute therapist support sessions) or standard charity support (SCS). Assessments were completed online pre-randomization, at 6- and 12-weeks post-randomization. Primary outcome was Patient Health Questionnaire Anxiety and Depression Scale; PHQ-ADS measured at 12-weeks. Analysis used intention-to-treat principles with adjusted mean differences estimated using linear mixed-effects models. Data-analyst was blinded to group allocation.

Results. 194 participants were randomized to COMPASS ($N = 94$) or SCS ($N = 100$). At 12-weeks, mean level of psychological distress was 6.82 (95% confidence interval; CI 4.55–9.10) points lower ($p < 0.001$) in the COMPASS arm compared with SCS (standardized mean difference of 0.71 (95% CI 0.48–0.95)). The COMPASS arm also showed moderate significant treatment effects on secondary outcomes including depression, anxiety and illness-related distress and small significant effects on functioning and quality-of-life. Rates of adverse events were comparable across the arms. Deterioration in distress at 12-weeks was observed in 2.2% of the SCS arm, and no participants in the COMPASS arm.

Conclusion. Compared with SCS, COMPASS digital therapeutic with minimal therapist input reduces psychological distress at post-treatment (12-weeks). COMPASS offers a potentially scalable implementation model for health services but its translation to these contexts needs further evaluating.

Trial Registration. NCT04535778

Introduction

An estimated 15.4 million people in England have one or more medical long-term condition(s) (LTCs). Thirty percent of these individuals have a comorbid mental health condition (Naylor et al., 2012, February 01). Comorbid depression in LTCs is related to worse prognosis and increased risk of mortality (Gold et al., 2020; Machado et al., 2018; Moussavi et al., 2007). Comorbid anxiety and/or depressive disorders increases physical healthcare costs by 45–75% (Naylor et al., 2012, February 01). Societal costs include increased work absence and disability leave (Hutter, Schnurr, & Baumeister, 2010; Naylor et al., 2016). Appropriate treatments for mental health in LTCs are estimated to reduce physical healthcare costs by 20% (Layard & Clark, 2015).

The main treatments for anxiety and depression in LTCs are psychotherapy and pharmacotherapy, alongside LTC management regimens (Gold et al., 2020). Pharmacotherapy is complicated by drug–drug interactions and contraindications in LTCs (Gold et al., 2020). Therefore, psychotherapy may be the treatment of choice. However, growing evidence shows that people treated with LTCs in primary mental health care services in England have poorer therapy outcomes for depression and anxiety than those without an LTC (Ewbank et al., 2020; Seaton, Moss-Morris, Norton, Hulme, & Hudson, 2022; Wakefield et al., 2021).

Preliminary evidence suggests treatment outcomes may be improved when treatment protocols are adapted to address the challenges of having an LTC (Wroe, Rennie, Sollesse, Chapman, & Hassy, 2018). CBT that integrates mental and physical health needs may increase treatment acceptability and patient engagement (Panchal, Rich, Rowland, Ryan, & Watts, 2020), and improve illness self-management behaviors (Wroe et al., 2018) which could cascade into improved clinical outcomes and reduced healthcare utilization.

However, providing access to psychological therapies tailored to the needs of people with LTCs is challenging from both the patient (e.g. time, travel, mobility) and health care provider perspectives (treatment costs and availability of adequately trained therapists) (Gandy et al., 2018; May et al., 2001). Digital therapies offer potential solutions to some of these challenges. Two meta-analytic reviews reported statistically significant small effects of digital therapies on depression and anxiety outcomes in LTC populations (Mehta, Peynenburg, & Hadjistavropoulos, 2019; White et al., 2022). Therapist-supported digital interventions showed larger treatment effects than unsupported interventions. Both reviews identified considerable heterogeneity across included studies in terms of the psychotherapy approach used, delivery format and the LTC populations studied.

Most evidence-based digital therapies for LTCs are disease-specific (Mehta et al., 2019; White et al., 2022) which limits the reach of the intervention and does not address challenges linked to multimorbidity. A recent randomized-controlled trial (RCT) ($n = 676$) evaluated the effectiveness of a digitally-delivered transdiagnostic (applying to any or multiple LTCs) psychological intervention with the support of a therapist (Dear et al., 2022). Moderate improvements in depression and small improvements in anxiety were demonstrated, providing support for a transdiagnostic approach to delivering integrated mental and physical health care. However, the theoretical underpinnings of the transdiagnostic intervention were not specified, the digital product did not appear to be interactive and tailored and may therefore require higher levels of therapist input. Lack of qualified therapists and costs associated with their time, mean wider implementation of this intervention may be challenging.

COMPASS: Navigating your long-term condition, is a digital therapeutic developed by researchers at King's College London using the UK Medical Research Council Complex Intervention Framework (Campbell et al., 2000; Moore et al., 2015). It is based on a transdiagnostic model of adjustment to LTCs (TMA-LTC) (Carroll, Moon, Hudson, Hulme, & Moss-Morris, 2022). The unique acute (e.g. relapse) and chronic stressors (e.g. unpleasant treatments) that people with LTCs face are at the core of this model. Using tailored and interactive pathways, COMPASS helps people build strategies to manage these stressors alongside strategies to manage mood. A preliminary implementation study was conducted in hospital services to ensure the product could work in routine care (Seaton, Moss-Morris, Hulme, Macaulay, & Hudson, 2023). Further improvements were made based on qualitative feedback from patients and therapists in this study. The aim of the current study was to test the efficacy of the product against a control group.

Primary objective

To assess the efficacy of COMPASS at reducing psychological distress based on the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS) (Kroenke et al., 2016) compared with standard charity support (SCS) alone at 12-weeks post-randomization.

Secondary objectives

To test the efficacy of COMPASS when compared to SCS at 12-weeks post-randomization on: depression, anxiety, functioning, quality of life, COVID-19-related distress, illness-related distress, knowledge and confidence for illness self-management, and perceived LTC symptom severity and improvement. Cost-effectiveness and nested qualitative research will be reported in separate publications.

Methods

Study design and participants

Two-armed parallel groups randomized controlled trial (RCT) with outcomes assessed at baseline, and 6- and 12-weeks (primary endpoint) after randomization. Participants were recruited through five national LTC UK charities, including: Crohn's & Colitis UK, Kidney Care UK, MS Society, Shift.ms and Psoriasis Association; between November 2020 and March 2021. These LTCs incorporate some different illness stressors and thus represent a range of physical health conditions. Data collection was completed in July 2021.

The trial protocol is published (Hulme et al., 2021) and registered on ClinicalTrials.gov (NCT04535778). This study is reported in line with the CONSORT guidance (online Supplementary File 01).

The following trial eligibility criteria were assessed via telephone:

Inclusion criteria

1. Aged ⩾18-years
2. Verbal and written proficiency in English
3. UK resident (GP registered)
4. Basic computer literacy with email address
5. Score of ⩾3 on the depression or anxiety items of PHQ-4 (Kroenke, Spitzer, Williams, & Löwe, 2009)
6. Self-reported diagnosis of LTC, confirmed by patient providing details of diagnosis (i.e. LTC, sub-type where applicable, when diagnosed, diagnosis confirmed by qualified medical practitioner)
7. Distress experienced is related to LTC (i.e. answer '*Yes*' or '*Sometimes*' to '*Is your distress related to your long-term condition?*')

Exclusion criteria

1. Self-report of existing substance dependency, moderate to severe cognitive impairment, severe mental health conditions (e.g. psychosis)
2. Suicidal risk: Identified by '*Yes*' to risk question ('*Are you currently making plans about how you would end your life?*')
3. Currently receiving psychological treatment from psychologist/counselor/therapist or online psychological treatment

Randomization and masking

After completing baseline assessments, participants were individually randomized using 1:1 allocation ratio, stratified by LTC

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to maintain balance across arms, to one of two trial arms using Qualtrics randomizer by an administrator independent of the trial team to maintain allocation concealment. A separate Qualtrics account was used for randomization and RedCap for outcome assessment to maintain blinding of the data analyst and to keep group allocation separate from questionnaire data.

As with any therapy trial, participants, therapists, and research assistants assisting with therapy arrangements could not be masked to treatment allocation. Outcomes were completed by participants independently of the study team online.

COMPASS intervention

COMPASS is a cognitive-behavioral program for psychological distress specific to LTCs (https://www.compass-ltc.org). It is CE-marked as a Class I Medical Device, in compliance with the Medical Devices Directive 93/42/EEC and consists of a platform for patients and a platform for therapists. Details of the 11 COMPASS treatment modules and how therapist support was provided alongside COMPASS are in the published protocol (Hulme et al., 2021).

Eight female therapists (mean age 30.8 years, range 24–45 years) provided COMPASS support including one welcome message and five 30-minute support calls. Five were trainee clinical/health psychologists and three were qualified clinical/health psychologists (37.5%) with a mean of 4.4 years (S.D. = 1.8, range 1–6 years) experience. Therapists received 2-days of training in clinical and technical aspects of COMPASS and working with LTC populations. Supervision (group and individual) was provided fortnightly by a Clinical Health Psychologist (AW). Fidelity to the COMPASS protocol was assessed using a bespoke therapist rating scale (online Supplementary File 02).

Intervention usage was automatically captured including number of online modules completed and mean duration of login. Adherence (adequate dose of treatment) was operationalized as undertaking ⩾3 telephone sessions/contacts and ⩾5 online COMPASS modules. Satisfaction with COMPASS was measured at 12-weeks post-randomization, by asking participants (i) if the intervention was helpful, (ii) if the intervention was relevant, and (iii) if the intervention was easy to use.

Treatment as usual – standard charity support (SCS)

SCS participants had access to support services and resources provided routinely by the charity. This differed across the charities, but may have included a helpline, online community support, counseling, financial support/grants, virtual events, and educational materials. Participants in the COMPASS arm were also able to access SCS. At each follow-up assessment, participants in both arms were asked what charity support they had accessed during the trial (type of support, number of times, and length of support received).

Following completion of the 12-weeks assessment, SCS only participants were sent a PDF of resources based on COMPASS content, signposting to online resources and outlining some basic tools for managing wellbeing.

Data collection

Outcome assessments were completed by participants on REDCap at baseline (pre-randomization), 6-weeks (mid-treatment), and 12-weeks (end-of-treatment; primary endpoint) after randomization.

Data on recruitment, retention, and reasons for drop-out were collected per CONSORT guidelines (Chan et al., 2013). Non-completers of the 12-weeks assessment were telephoned to complete the primary outcome measure after three reminders by a member of the research team blinded to treatment allocation.

Socio-demographic and clinical data were collected at baseline, including: age, gender, ethnicity, employment status, occupation type, education level, marital status, living arrangements, type of LTC, and comorbidities. Postcodes were used to calculate level of deprivation using the Ministry of Housing, Communities and Local Government English indices of deprivation (Noble et al., 2019, September 01).

Outcomes

Primary outcome: Distress was measured using the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS) (Kroenke et al., 2016) which includes the Patient Health Questionnaire (PHQ-9) (Kroenke & Spitzer, 2002) and the Generalized Anxiety Disorder Scale (GAD-7) (Spitzer, Kroenke, Williams, & Löwe, 2006). Items are rated on a Likert Scale (0–3) with scores ranging from 0 to 48. Higher scores indicate higher distress. A change of ⩾4 is considered a minimum clinically important difference (MCID) (Kroenke et al., 2016). Cut-offs of 10, 20, and 30 indicate mild, moderate, and severe levels of distress respectively (Kroenke et al., 2016). The PHQ-ADS has high internal reliability and sensitivity to change (Kroenke et al., 2016). Cronbach's alpha here was 0.91.

A combined score for depression and anxiety (Kroenke et al., 2016) was selected to be our primary measure because: (1) symptoms of depression and anxiety often co-occur, (2) some patients may be experiencing subthreshold levels of depression and anxiety, but together the level of psychological symptomatology may be clinically meaningful to warrant treatment and (3) COMPASS was designed to be transdiagnostic i.e. treat symptoms of both depression and anxiety. The effect of the intervention on depression and anxiety separately was also evaluated as part of secondary outcomes (see below) to ascertain if the effects on each of the mood measures is roughly equivalent.

Secondary outcomes:

- **Depression** (PHQ-9; Kroenke and Spitzer, 2002); Cronbach's alpha here 0.84.Cut-offs of 5, 10, and 15 represent mild, moderate, and severe depression.
- **Anxiety** (GAD-7; Spitzer et al., 2006); Cronbach's alpha here 0.86. Cut-offs of 5, 10, and 15 represent mild, moderate, and severe anxiety.
- **Daily functioning** (Work and Social Adjustment Scale, WSAS; Mundt, Marks, Shear, and Greist, 2002); Cronbach's alpha here 0.82.
- **COVID-19-related distress** (six-item emotional representations subscale from the Illness Perceptions Questionnaire-Revised - IPQ-R; Moss-Morris et al., 2002 where items were rated specfic to emotional reponses to Covid pandemic); Cronbach's alpha here 0.83.
- **Illness-related distress** (IRD: bespoke 2-item measure, resembling PHQ-9 and GAD-7); Cronbach's alpha here 0.81.
- **Knowledge and confidence for illness self-management** (13-item Patient Activation Measure - PAM short version; Hibbard, Mahoney, Stockard, and Tusler, 2005); Cronbach's alpha here 0.83.

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- **LTC symptom severity** (single-item Patient Global Impression Scale of Severity - PGI-S; Yalcin and Bump, 2003).
- **Improvement in LTC symptoms** (single-item Patient Global Impression Scale of Improvement - PGI-I Yalcin and Bump, 2003). This item was only collected at 6- and 12-weeks post-randomization, but not at baseline.
- **Quality of life** (European Quality of Life Scale - EQ-5D-3L; Rabin and Charro, 2001). As part of analysis converted to EQ-5D-5L index value scores.

Except for the PAM and EQ-5D, greater scores indicted worse/poorer outcomes.

Adverse events Deterioration in distress was classed as an adverse event based on increase in 6 on the PHQ and 4 on the GAD.

Self-reported life-threatening events, unplanned hospitalizations, events resulting in permanent disability/incapacity, any other physical or mental health events requiring medical attention, and personal circumstance events (e.g. bereavement) were also included in the 12-week follow-up questionnaire based on guidelines for standard reporting of adverse events in clinical trials, particularly of psychological therapies (Duggan, Parry, McMurran, Davidson, & Dennis, 2014; Ioannidis et al., 2004). For those in the COMPASS arm, therapists reported any possible serious adverse events that were mentioned by participants to KH, one of the trial co-ordinators. KH completed the serious adverse events document and discussed with the Trial Supervisor (AW). If deemed possibly related to the therapy, the event was to be reported to the ethics committee.

Further information on all measures used, including those not reported here that will be used in additional linked papers, is available in the protocol (Hulme et al., 2021).

Sample size

We powered to detect a standardized mean difference (SMD) 0.40 on the PHQ-ADS (Kroenke et al., 2016) between arms at 12-weeks post-randomization. To achieve 80% power, at 5% significance level, and inflating for 15% attrition, required 196 participants, rounded up to 200. A SMD of 0.40 was selected as a 4-point difference on the PHQ-ADS (S.D. = 10) represents the MCID (Kroenke et al., 2016).

Statistical analysis

An intention-to-treat (ITT) approach was used following a pre-specified analysis plan in Stata 16.1. The treatment effect of the intervention on the primary outcome at 6-weeks and 12-weeks post-randomization (primary endpoint) was estimated using a linear mixed-effects model. A random effect for participants was included to account for repeated assessment of outcomes within individuals and a random effect for therapists was included to account for partial clustering. Robust standard errors following the Huber-White method were used to protect against deviations from normality and homoscedasticity of residuals. To calculate treatment effect estimates at 12-weeks post-randomization, time and treatment group were included as dummy coded covariates along with time by treatment group interaction terms. Unstandardized and standardized (Hedge's g) treatment effect estimates (Standardized Mean Difference in the Results section) are presented with 95% confidence intervals. Stratification variable used in the randomization (i.e. LTCs) and baseline level of the outcome were included as covariates.

Descriptive analyses were undertaken to aid the interpretation of the treatment effect on the primary outcome. Specifically, changes in the primary outcome (PHQ-ADS) indicative of improvement based on the MCID of 4 points or deterioration based on an increase in 6 on the PHQ and 4 on the GAD (Kroenke et al., 2016) were tabulated and graphically presented per Jacobson and Truax's reliable change index method (Jacobson & Truax, 1991).

Secondary continuous outcomes, were analyzed using linear-mixed effects models following the approach described above. The PGI-S and PGI-I are ordinal scales and were analyzed using mixed-effects proportional odds models, including the same covariates as specified above. For the PGI-I the baseline level of the variable was not included as a covariate since it was not collected.

Planned sensitivity analyses on the primary outcome (PHQ-ADS) involved consideration of the impact of missing follow-up data, including: (1) assessments completed outside of specified range from due date (no more than 7 days before the expected due date of follow-up and no more than 28 days after the expected due date of follow-up), (2) 12-weeks assessments completed over the phone, (3) pattern-mixture model incorporating a baseline value (plus or minus a plausible range of values, defined as 5 here, and baseline observation carried forward imputation), (4) no longer meeting diagnostic caseness at baseline (<10 on PHQ-ADS), and (5) controlling for baseline variables associated with missingness (specifically age, gender, education, marital status, and use of psychotropic medication).

Moderator analyses were conducted to examine treatment effect heterogeneity for baseline variables which may affect treatment outcome, including age, baseline PHQ-ADS, LTC type, and ethnicity. Analysis for each putative moderator included the main effect and a treatment group by moderator interaction term in the mixed-effects model used to estimate the treatment effect for the primary outcome, based on the intention-to-treat sample. Pre-specified mediation analysis was not performed because there was no significant treatment effect on the PAM at both timepoints.

Results

Recruitment and retention overview

194 of 252 patients (77.0%) screened for eligibility were recruited. Demographic information and type of LTC are shown in Table 1. Figure 1 displays the CONSORT flow diagram. Follow-up rates were: 73.7% (143/194) at 6-weeks and 83.5% (162/194) at 12-weeks. The rate of attrition at 12-weeks was higher in the COMPASS arm (24.5%) compared to the SCS arm (9.0%).

Baseline characteristics

Table 1 shows participants' baseline characteristics by trial arm. The sample was predominantly female and white, but there was a spread across the least to most deprived socio-economic deciles.

The baseline mean scores on the primary and secondary outcomes can be seen to Table 2. All baseline characteristics appeared balanced between groups. Table 1 shows the breakdown for anxiety and depression using the cut-offs for none, mild, moderate, and severe on PHQ-9 and GAD-7. 72.7% of the sample reported moderate or severe anxiety or depression on one or both

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Table 1. Baseline characteristics of sample ($N = 194$)

		COMPASS $N = 94$	SCS $N = 100$
Age (M, s.d.)		40.9 (12.7)	41.0 (13.7)
Gender (N, %)*	Male	18 (19.1%)	22 (22.0%)
	Female	75 (79.8%)	78 (78.0%)
	Prefer not to say	1 (1.1%)	0 (0.0%)
Ethnicity (N, %)*	White	87 (92.6%)	93 (93.0%)
	Black	1 (1.1%)	0 (0.0%)
	Asian	5 (5.3%)	4 (4.0%)
	Mixed	1 (1.1%)	3 (3.0%)
Long-term condition (N, %)	Psoriasis	7 (7.4%)	7 (7.0%)
	Inflammatory bowel disease	46 (48.9%)	50 (50.0%)
	Chronic kidney disease	24 (25.5%)	26 (26.0%)
	Multiple sclerosis	17 (18.1%)	17 (17.0%)
Number of comorbidities (M, s.d.)		1.6 (1.8)	1.3 (1.5)
Education (N, %)*	High school	32 (34.0%)	27 (27.0%)
	Undergraduate/postgraduate	50 (53.2%)	61 (61.0%)
	Other	12 (12.8%)	12 (12.0%)
Employment (N, %)*	Employed	57 (60.6%)	62 (62.0%)
	Long-term sick or disabled	15 (16.0%)	9 (9.0%)
	Other	22 (23.4%)	29 (29.0%)
Living arrangements (N, %)*	Living alone	16 (17.0%)	10 (10.0%)
	Living with partner/children	63 (67.0%)	73 (73.0%)
	Other	15 (16.0%)	17 (17.0%)
Occupation (N, %)*	Professional occupations	29 (30.9%)	34 (34.0%)
	Admin and secretarial occupations	20 (21.3%)	19 (19.0%)
	Other	45 (47.9%)	47 (47.0%)
Marital status (N, %)*	Married	37 (39.4%)	44 (44.0%)
	Single	26 (27.7%)	26 (26.0%)
	Other	31 (33.0%)	30 (30.0%)
Use of psychotropic medication (N, %)*	Prescribed and taking	32 (34.0%)	24 (24.0%)
	Prescribed but not taking	3 (3.2%)	5 (5.0%)
	Not prescribed	58 (61.7%)	70 (70.0%)
	Not sure	1 (1.1%)	1 (1.0%)
Receipt of sick pay (N, %)*	Yes	1 (1.1%)	4 (4.0%)
	No	91 (96.8%)	95 (95.0%)
	Unsure / prefer not to say	2 (2.1%)	1 (1.0%)
IMD decile (Median, IQR)		6.0 (4.0-9.0)	6.0 (4.0-8.0)
PHQ categories (N, %)	Minimal	7 (7.4%)	10 (10.0%)
	Mild	21 (22.3%)	31 (31.0%)
	Moderate	36 (38.3%)	26 (26.0%)
	Severe	30 (31.9%)	33 (33.0%)
GAD categories (N, %)	Minimal	4 (4.3%)	9 (9.0%)
	Mild	34 (36.2%)	39 (39.0%)

(*Continued*)

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Table 1. (*Continued.*)

		COMPASS $N = 94$	SCS $N = 100$
	Moderate	33 (35.1%)	32 (32.0%)
	Severe	23 (24.5%)	20 (20.0%)
PAM Levels of activation (*N*, %)	1	31 (33%)	39 (39%)
	2	23 (24%)	21 (21%)
	3	34 (36%)	27 (27%)
	4	6 (6%)	12 (12%)

Note. *In the protocol, description of PAM's scoring was based on https://doi.org/10.1016/j.pec.2015.06.009. Post publication of the protocol, we obtained the PAM license scoring algorithm. This produces a continuous score from 0-100 that correlates to one of four levels of patient activation (Levels 1 and 2 indicate lower patient activation, while PAM Levels 3 and 4 indicate higher patient activation). Descriptive statistics for patient activation levels are provided here. Continuous scoring only (see Table 2 for M S.D.) was used to estimate efficacy.

measures. Mean WSAS (functional impairment) at baseline across the two arms was 21.58 (S.D. = 8.27) suggesting significant functional impairment. PAM Categories showed that 59% of patients fell into categories 1 and 2 suggesting they were overwhelmed or struggling with illness self-management.

Missingness

Group differences on baseline variables between those included in the analysis sample ($N = 168$) and those who did not provide any post-randomization assessment data ($N = 26$), and thus not possible to include in the analysis, are available in online Supplementary File 03. Those not providing any post-randomization assessment data were, on average, significantly younger, had lower levels of education, more likely to be taking psychotropic medication, and had worse baseline levels of distress.

Acceptability, adherence to COMPASS, and treatment fidelity

In the COMPASS arm, five participants dropped out of treatment (5.3%), COMPASS session acceptability was rated out of five for helpfulness ($M = 4.17$, S.D. = 1.0), relevance ($M = 4.29$, S.D. = 0.93) and ease of navigation ($M = 4.21$, S.D. = 1.1). Participants spent a median of 144 min on COMPASS (IQR = 48.8–294.5) averaging 5.81 (S.D. = 3.6) completed sessions. Mean attendance at telephone sessions was 3.91 (S.D. = 1.7), an average of 2.25 therapist hours (S.D. = 1.07). Regarding adherence, 58 (61.7%) met the composite adherence definition: 70 (74.4%) adhered to the therapist appointment criterion (⩾3 appointments) and 59 (62.8%) adhered to the session recommendation (⩾5 sessions). Those non-adherent to COMPASS were more likely to have Chronic Kidney Disease (CKD) (online Supplementary File 04).

Therapist treatment fidelity ratings are in online Supplementary File 05. Fidelity to COMPASS specific skills was excellent/extensive. General CBT fidelity was rated slightly slower ranging from good to excellent. 177/369 (48%) of sessions delivered were over 30 min suggesting therapists had difficulty sticking to the time limit.

Charity support accessed

The frequency and type of charity support accessed was generally comparable across the arms (online Supplementary File 06).

Treatment effects

Table 2 shows the group means at each assessment and adjusted mean differences between groups at the two post-randomization assessments for primary and secondary continuous outcomes using the intention-to-treat sample. Figure 2 presents a forest plot of the treatment effects.

Primary outcome measure

Compared with SCS, at 12-weeks distress was 6.82 (95% CI 4.55–9.10) points lower ($p < 0.001$) in the COMPASS arm, with a Standardized Mean Difference (SMD) of 0.71. At 12-weeks 63/71 (88.7%) of participants in the COMPASS arm reported a clinically significant change in PHQ-ADS compared to 41/91 (45.1%) in the SCS arm.

Secondary outcome measures

Table 2 shows medium to large significant treatment effects (SMD range 0.45 to 0.70) were observed in favor of COMPASS at 12-weeks on the following secondary outcomes: PHQ-9, GAD-7, and IRD (illness-related distress). Small significant treatment effects were observed in favor of COMPASS at 12-weeks on the WSAS (SMD = 0.30) and the EQ-5D-5L (SMD = 0.17). There was a small non-significant difference (SMD = 0.28) favoring the COMPASS arm on the PAM at 12-weeks. Likewise, there was a small non-significant difference in COVID-related distress at 12-weeks post-randomization.

Table 3 shows a breakdown of responses on the PGI-S and PGI-I by group and time, as well as the inferential data for the group differences. There was no significant difference between the groups on the PGI-S or PGI-I at 12-weeks.

Sensitivity analyses

Planned sensitivity analyses using the primary outcome (PHQ-ADS) are reported in online Supplementary File 07. Across the sensitivity analyses, the treatment effects on the primary outcome were generally consistent with the intention-to-treat analysis, confirming the robustness of the treatment effect in relation to different assumptions concerning missing outcome data.

Controlling for variables associated with missingness, the treatment effect on PHQ-ADS was 0.74 (95% CI 0.50–0.98) compared with 0.71 (95% CI 0.48–0.95) for the main analysis. Missing not at random sensitivity analysis indicated that, even under the

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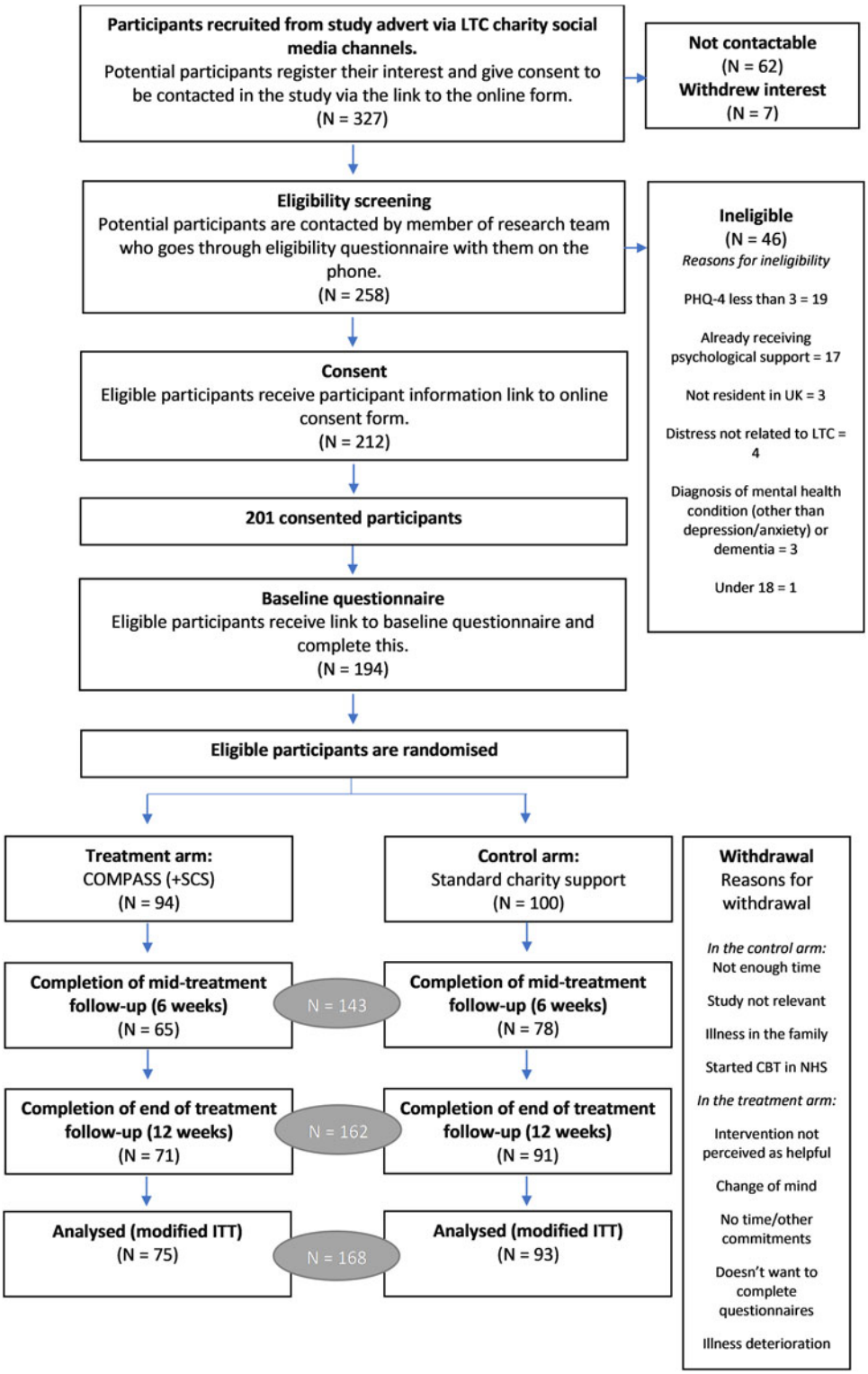

Figure 1. CONSORT flow diagram.

conservative scenario, assuming those with missing data worsened by 5-points, treatment effect estimates at 12-weeks were reduced only to 0.47 (95% CI 0.15–0.79) and remained statistically significant. Furthermore, treatment effects using the per-protocol sample (those who received adequate dose of treatment previously specified) were comparable to the intention-to-treat sample (SMD = 0.63; 95% CI 0.42–0.84).

Moderation analysis

There was no statistically significant heterogeneity of treatment effects on the PHQ-ADS at 12-weeks by age, baseline PHQ-ADS, LTC type, and ethnicity (online Supplementary File 08). Although the interaction effect of baseline distress was not significant, a trend was observed where for each one-point

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Table 2. Treatment effects on primary and secondary continuous outcomes

		COMPASS			SCS			Adjusted mean difference								
Variable	Time	*N*	Mean	S.D.	*N*	Mean	S.D.	Mean diff	S.E.	*z*	*p*	95%ll	95% ul	SMD	95%ll	95% ul
PRIMARY OUTCOME																
Distress (PHQ-ADS)	1	75	22.76	9.46	93	21.62	9.69									
	2	**65**	**16.08**	**10.41**	**78**	**21.09**	**10.73**	**5.07**	**1.28**	**3.96**	**<0.001**	**2.56**	**7.58**	**0.53**	**0.27**	**0.79**
	3	**71**	**12.32**	**8.15**	**91**	**18.27**	**11.07**	**6.82**	**1.16**	**5.88**	**<0.001**	**4.55**	**9.10**	**0.71**	**0.48**	**0.95**
SECONDARY OUTCOMES																
Depression (PHQ-9)	1	75	11.72	5.36	93	11.57	5.90									
	2	**65**	**8.15**	**5.85**	**78**	**11.18**	**6.29**	**2.55**	**0.73**	**3.49**	**<0.001**	**1.12**	**3.99**	**0.45**	**0.20**	**0.71**
	3	**71**	**6.72**	**4.82**	**91**	**9.99**	**6.60**	**3.49**	**0.63**	**5.54**	**<0.001**	**2.25**	**4.72**	**0.62**	**0.40**	**0.84**
Anxiety (GAD-7)	1	75	11.04	4.83	93	10.05	4.52									
	2	**65**	**7.92**	**4.87**	**78**	**9.91**	**5.08**	**2.44**	**0.63**	**3.89**	**<0.001**	**1.21**	**3.66**	**0.52**	**0.26**	**0.78**
	3	**71**	**5.61**	**3.78**	**91**	**8.29**	**5.20**	**3.26**	**0.64**	**5.07**	**<0.001**	**2.00**	**4.51**	**0.70**	**0.43**	**0.97**
Functional impairment (WSAS)	1	75	21.73	8.84	93	21.30	8.29									
	2	**65**	**18.73**	**8.47**	**76**	**21.13**	**9.51**	**2.14**	**0.87**	**2.47**	**0.013**	**0.44**	**3.84**	**0.25**	**0.05**	**0.45**
	3	**66**	**17.34**	**9.12**	**86**	**19.16**	**9.90**	**2.58**	**1.01**	**2.56**	**0.010**	**0.61**	**4.56**	**0.30**	**0.07**	**0.54**
Illness-related distress (IRD)	1	75	3.09	1.75	93	2.77	1.82									
	2	**65**	**1.92**	**1.58**	**78**	**2.76**	**1.83**	**0.91**	**0.19**	**4.75**	**<0.001**	**0.54**	**1.29**	**0.51**	**0.30**	**0.72**
	3	**66**	**1.59**	**1.46**	**86**	**2.40**	**1.89**	**1.01**	**0.22**	**4.52**	**<0.001**	**0.57**	**1.45**	**0.56**	**0.32**	**0.81**
COVID-related distress (IPQ-R emotional representations subscale)	1	75	22.53	4.90	93	22.65	4.77									
	2	**65**	**21.26**	**5.00**	**76**	**22.21**	**4.72**	**0.68**	**0.33**	**2.05**	**0.040**	**0.03**	**1.33**	**0.14**	**0.01**	**0.28**
	3	66	19.91	5.03	85	21.05	5.03	0.65	0.49	1.34	0.180	−0.30	1.61	0.14	−0.06	0.34
Knowledge and confidence to self-manage LTC (PAM)	1	75	54.57	11.62	92	53.95	11.82									
	2	64	56.36	11.68	74	55.80	13.69	0.10	1.84	0.06	0.956	−3.51	3.71	−0.01	0.30	−0.32
	3	66	60.18	14.22	84	56.18	12.87	−3.29	2.22	−1.49	0.137	−7.63	1.05	0.28	0.65	−0.09
Quality of life (EQ-5D-5L)	1	75	0.67	0.19	93	0.64	0.21									
	2	**65**	**0.72**	**0.19**	**76**	**0.62**	**0.23**	**−0.05**	**0.02**	**−2.79**	**0.005**	**−0.09**	**−0.01**	**0.25**	**0.42**	**0.07**
	3	**66**	**0.73**	**0.18**	**85**	**0.66**	**0.23**	**−0.04**	**0.02**	**−2.14**	**0.033**	**−0.07**	**0.00**	**0.17**	**0.33**	**0.01**

Notes. Negative SMD indicates effect in favor of SCS arm. Bold text denotes significant differences between arms.

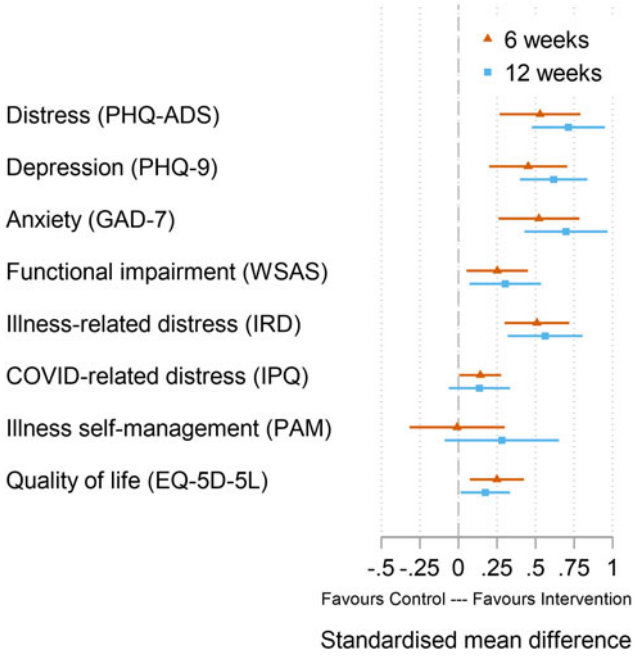

Figure 2. Forest plot of treatment effects with 95% CIs.

increase in baseline distress, there was a 0.18 increase in treatment effect on the PHQ-ADS at 12-weeks.

Adverse events

Figure 3 shows the clinically meaningful change for both improvement and deterioration in PHQ-ADS, PHQ-9, and GAD-7 from baseline to post-randomization using the ITT sample by group as per Jacobson & Truax's (1991) reliable change index method. Across the three outcomes, data were clustered on the improvement side of the no change line, particularly among COMPASS participants. A few participants displayed deterioration at follow-up, predominantly in the SCS arm. At 6-weeks post-randomization, across distress, depression, and anxiety, the percentage of COMPASS participants displaying a deterioration ranged from 1.5% to 7.7%, while in the SCS arm this ranged from 3.9% to 15.4%. At 12-weeks post-randomization, across the three outcomes, the percentage of COMPASS participants displaying a deterioration ranged from 0% to 1.4%, while in SCS this ranged from 2.2% to 11.0%. Deterioration was more common in the SCS arm compared to the COMPASS arm across both post-randomization timepoints.

Self-reported adverse events reported in the 12-week questionnaire by group are summarized in Table 4. Rates of adverse events were comparable across the two arms. Only three serious adverse events were mentioned by patients in the therapy arm. All were related to hospital admissions, one because of COVID-19 and two because of relapse of physical illness. To the best of our knowledge these were unrelated to the COMPASS intervention.

Discussion

Patients randomized to COMPASS, therapist-guided online CBT for treating anxiety and depression associated with living with an LTC, showed greater improvements on most outcomes when compared to those who had SCS alone. A moderate treatment effect (SMD = 0.71) in favor of COMPASS was observed on the primary outcome, distress (PHQ-ADS) with 89% of the COMPASS arm showing a clinically significant change from baseline compared to 45% of the SCS.

Of the 9 secondary outcomes measured, five showed statistically significant effects in favor of COMPASS at 12-weeks. Moderate effects were found for depression (PHQ-9) and anxiety (GAD-7) when analyzed separately, and small improvements in favor of COMPASS were also found on functional impairment (WSAS), illness-specific distress, and quality-of-life (EQ-5D-5L). There were no significant differences between groups on the two single-item measures; LTC symptom severity and improvement, or on the knowledge and confidence to self-manage the LTC (PAM).

The effect size on the primary outcome in this RCT is larger than the small to moderate effect sizes reported in systematic reviews of digital CBT for treating depression and anxiety in LTCs (Mehta et al., 2019; White et al., 2022). Most interventions in these meta-analyses were disease-specific. COMPASS was developed to transdiagnostically treat both anxiety and depression, as well as addressing core illness-related challenges across LTCs. As similar moderate effect sizes were found when anxiety and depression were analyzed separately, and there was no clear moderator effect for type of LTC, COMPASS appears to achieve its transdiagnostic aims.

As far as we are aware, there is only one other published RCT of a digital intervention (Dear et al., 2022) with a transdiagnostic treatment for depression and anxiety across LTCs. This RCT compared 8-weeks of a transdiagnostic, therapist-supported digital intervention for LTCs to a wait-list control arm. Moderate treatment effects for depression and small effects for anxiety were reported. Our reported effect sizes appear slightly larger which may reflect trial or treatment differences. Taken together, these RCTs suggest a transdiagnostic approach is effective for treating distress in LTCs and can be delivered with minimal therapist time. In this RCT, COMPASS users had maximum of five sessions with their guide. These were designed as 30-minute sessions although some sessions overran, particularly with the less experienced therapists who took a bit of time to get used to the 30-minute session limit. This is still half the time patients with anxiety and depression routinely receive in NHS England Improving Access to Psychological Therapy services when offered low intensity treatment which typically consists of six to eight one-hour sessions.

In terms of acceptability of COMPASS, drop out was low (5%) and patient rating positive. 61.7% of the sample adhered to the treatment protocol as intended. This is comparable with the findings from a meta-analysis of 12 digitally-delivered CBT interventions which reported adherence rates of 65% (Van Ballegooijen et al., 2014). Of note, however, adherence rates varied across LTC populations with the lowest adherence rates observed in the CKD group. As COMPASS is transdiagnostic, it may miss some of the more specific disease management strategies (e.g. fluid management in kidney disease) and this may cause people to feel key relevant content is missing and thus disengage. This may also explain why the treatment gains on efficacy to manage their LTC were not significantly different across the groups. Incorporating some disease-specific management may further enhance COMPASS effects for specific conditions and promote adherence.

Although the intervention was low intensity in terms of therapist time (2.5 h in total), over 70% of the sample included in

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Table 3. Treatment effects on secondary ordinal outcomes

			Group 1 ($n = 73$)		Group 2 ($n = 91$)		Treatment effect								
		Time	*N*	%	*N*	%	Logit	se	*z*	*p*	95%ll	95%ul	OR	95%ll	95%ul
PGI-S	1	Baseline	8	8.6	4	4.0									
	2		18	19.4	31	31.0									
	3		50	53.8	46	46.0									
	4		17	18.3	19	19.0									
	1	6 weeks	2	3.2	8	10.5	0.13	0.45	0.29	0.771	−0.75	1.01	1.14	0.47	2.73
	2		25	39.7	17	22.4									
	3		27	42.9	42	55.3									
	4		9	14.3	9	11.8									
	1	12 weeks	6	9.1	13	15.3	0.37	0.48	0.78	0.438	−0.57	1.31	1.45	0	3.72
	2		22	33.3	18	21.2									
	3		27	40.9	40	47.1									
	4		11	16.7	14	16.5									
PGI-I	1	6 weeks	0	0	0	0	**−1.25**	**0.55**	**−2.29**	**0.022**	**−2.33**	**−0.18**	**0.29**	**0.10**	**0.83**
	2		6	9.5	1	1.3									
	3		19	30.2	11	14.5									
	4		24	38.1	39	51.3									
	5		11	17.5	17	22.4									
	6		3	4.8	7	9.2									
	7		0	0	1	1.3									
	1	12 weeks	1	1.5	2	2.4	−0.78	0.57	−1.37	0.171	−1.90	0.34	0.46	0.15	1.40
	2		10	15.2	7	8.2									
	3		25	37.9	8	9.4									
	4		21	31.8	40	47.1									
	5		8	12.1	25	29.4									
	6		0	0	2	2.4									
	7		1	1.5	1	1.2									

Notes. OR below 1 indicates effect in favor of COMPASS arm. Bold text denotes significant differences between arms.

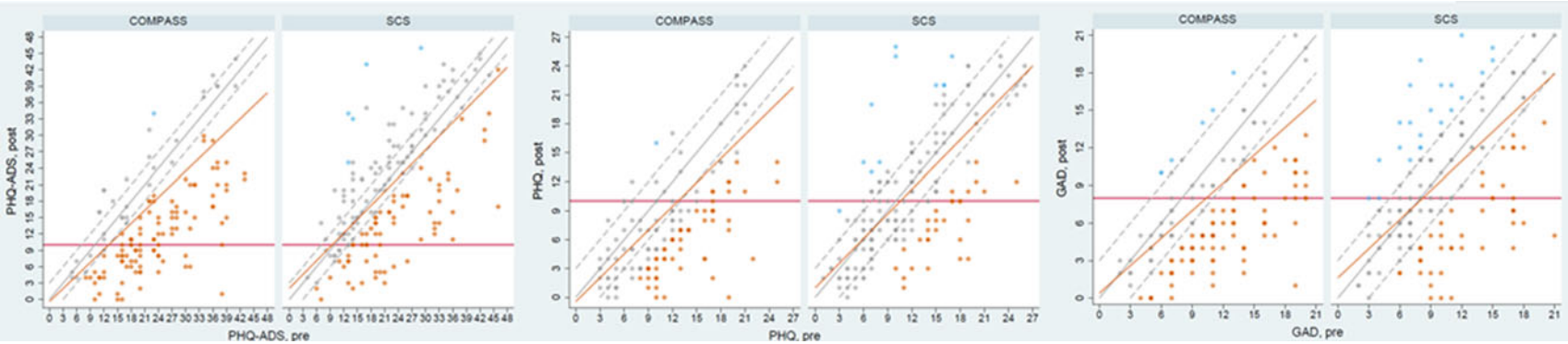

Figure 3. Change in distress (PHQ-ADS), depression (PHQ-9), and anxiety (GAD-7) by trial arm (ITT sample) to assess reliable deterioration and improvement. Scatterplots of observations according to level of change, where (1) blue dots represent deterioration (increase of ⩾6 points on PHQ-9 and/or an increase of ⩾4 points on GAD-7), (2) orange dots represent improvement (a reduction of ⩾4 points on PHQ-ADS and GAD-7 considered as a minimum clinically important difference and a reduction of ⩾6 points on PHQ-9 considered as a minimum clinically important difference), and (3) gray dots represent change that falls outside of these criteria of deterioration or improvement. The solid gray line represents no change with the 95% confidence interval displayed by the dotted gray lines. The solid red line displays the cut-off scores on each scale suggestive of probable clinical levels of distress/depression/anxiety, respectively (PHQ-ADS ⩾10, PHQ-9 ⩾10, and GAD-7 ⩾8). The solid orange line presents the reliable change index by trial arm based on the level of deterioration and improvement.

Table 4. Self-reported adverse events at 12-weeks post-randomization by arm

	COMPASS $N = 67$	SCS $N = 87$	*p*-value
Life threatening	2 (3.0%)	4 (4.6%)	0.61
Hospital admission	6 (9.0%)	9 (10.3%)	0.77
Event resulting in permanent disability or incapacity	0 (0.0%)	1 (1.1%)	0.38
Other physical health event	20 (29.9%)	20 (23.0%)	0.34
Other mental health event	2 (3.0%)	6 (6.9%)	0.28
Event related to circumstances	23 (34.3%)	27 (31.0%)	0.67
None of these adverse events	33 (49.3%)	40 (46.0%)	0.69

this study had moderate to severe anxiety and/or depression at baseline, using recognized clinical cut-offs on the PHQ-9 and GAD-7. Therefore, COMPASS was not just targeting the mild to moderate mood severity group, which in England is the group who would traditionally receive lower intensity treatments (NHS England, 2018, June 01). It is consistent with the findings of an individual patient data meta-analysis ($n = 2470$) which observed that people with severe depression at baseline had equivalent clinical gains in depression outcomes when exposed to low intensity interventions (e.g. less therapist support time) compared with those with less severe depression (Bower et al., 2013). Thus, therapist-supported digital delivery of treatments to people with moderate to severe symptoms of depression and anxiety in LTCs is likely a scalable model of implementation. This trial also provides support for an alternative delivery pathway through a national hub linked to self-referral through charities, rather than as part of regional primary or secondary care. This delivery pathway could alleviate the demand on charities who already provide some essential support services, and enable them to facilitate access to further specialized treatment.

Limitations of this study include the recruitment strategy through social media which may have limited the representativeness of the sample, which was largely white, and likely technologically literate. Whilst patient choice is essential for successful treatment plans, referrals to online programs should only occur when patients are comfortable with this therapy medium. Another limitation was recruiting through LTC charities relating to only four illnesses (MS, psoriasis, kidney disease, and IBD). However, the LTCs selected spanned different bodily systems and had different disease presentations (relapsing-remitting, progressive, or constant). In addition, comorbid conditions were frequently reported in our sample, suggesting LTC diversity. There was also more drop-out in the COMPASS arm with some systematic differences between patients retained and those who dropped out across the whole sample, indicative of attrition bias; however, evaluation of the impact of missingness on the treatment effect on the primary outcome demonstrated the robustness of the results. Follow-up data as part of this study was limited to post-treatment (12-weeks post-randomization), so further research is needed to ascertain if treatment effects are sustained.

A strength of this study is that it was delivered during COVID-19 pandemic, without any input from already overstretched healthcare services. The centralized model used, with remote support, requires minimal implementation, and where therapists receive high quality training and supervision, proved to be efficacious as well as rapid to implement. The therapists ranged considerably in terms of experience. Providing training in the COMPASS specific approach and regular group supervision assured good fidelity to the approach and may have contributed to the positive outcomes.

Currently there is no LTC transdiagnostic digital therapy program available in national healthcare services in England. COMPASS is CE-marked so meets current requirements for implementation as a Class 1 medical device. It is undergoing further study using implementation science methods in two IAPT services in England. More tailored versions for IBD and MS are being developed to explore implementation in secondary care services as well as to enhance illness specific self-management. Patient and healthcare professionals' input to ongoingly enhance COMPASS is at the heart of all further studies.

Conclusion

COMPASS appears an effective treatment for psychological distress related to living with LTCs with significant moderate effects on both depression and anxiety. Findings highlight the relevance of tailoring psychological interventions to LTCs and show that delivering care via interactive, tailored digital therapeutics is viable. It also presents a novel implementation pathway, i.e. via a centralized Hub, which warrants further exploration as a future implementation model.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291723003756.

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Competing interests. RMM receives payment for consultancy to Mahana Therapeutics, has share options in Mahana therapeutics, and is a beneficiary of a license agreement for a digital CBT program for irritable bowel syndrome between Mahana therapeutics and King's College London.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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