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A pilot randomised controlled trial of the Tailored Intervention for people with moderate-to-severe Chronic Obstructive Pulmonary Disease and Co-morbidities delivered by Pharmacists and Consultant respiratory Physicians (TICC-PCP)

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To achieve progression criteria for a definitive phase three randomised controlled trial (RCT). Prospective phase two multicentre parallel-group RCT. Participants recruited from secondary care respiratory clinics in two health boards in Scotland, United Kingdom. 110 adults with moderate-severe COPD and co-morbidities. Tailored Intervention for COPD and Co-morbidities by Pharmacists and Consultant Physicians (TICC-PCP): home visits (for a year) by generalist prescribing pharmacists collaborating with consultant respiratory physicians. Pharmacists assessed, prescribed, de-prescribed, and referred participants to health and social care services as appropriate, in addition to Usual Care (UC). Recruit ≥100 participants; deliver TICC-PCP to ≥70% intervention-arm participants; collect ≥90% in-person data; retain ≥80% participants until 21-months. Secondary outcomes include clinical and health service utilisation. Recruitment, data collection, retention and participant retention targets were achieved over 21 months. TICC-PCP delivery: the median number of contacts, nine per participant in one year, matched the a-priori target although fewer than expected (13 (27%)) received the planned schedule of contacts (monthly for six months then every other month for six months). Secondary outcomes included increased prescribing of bone strengthening medicines, de-prescribing of medicines associated with increasing falls risk; delayed time to emergency health care contacts, fewer exacerbations; improved health related quality of life and longer duration of hospitalisation. A definitive phase three RCT of TICC-PCP may improve outcomes for people with moderate-severe COPD and co-morbidities. Trial registration: The trial is registered with the UK Clinical Trials Registry (https://doi.org/10.1186/ISRCTN43508703). Registration date: 3/1/2020.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a growing global health problem associated with substantial morbidity, mortality and economic costs[1]. COPD has a symptom burden comparable with lung cancer[2], and most patients live with multiple comorbidities requiring lifelong treatment and review[3]. People living at home with symptomatic COPD are often housebound due to breathlessness, prone to psychological distress, with multiple unmet health and social care needs[4,5]. Co-morbidities worsen outcomes, increase health service costs, and require lifelong polypharmacy that increases the risk of adverse drug reactions (ADRs)[3] suggesting a need for cost-effective home-based holistic interventions by generalists who can address comorbidities alongside COPD[6].

Despite recommendations that COPD disease management programmes should address comorbidities and wider health determinants[7], randomised controlled trial (RCT) evidence of home-based Interventions is scarce[8]. General Practitioner (GP) home visits are increasingly delegated to other healthcare professionals (HCPs)[9]. Worldwide, HCPs have undergone training to become Independent Prescribers (IP)[10], enabling clinical assessment and autonomous prescribing within their competence[11]. Generalist IP pharmacists can improve prescribing and may improve clinical outcomes, in targeted groups of patients[12,13].

In a non-randomised feasibility study, a Tailored, home-based Intervention for people with COPD and comorbidities by generalist prescribing Pharmacists collaborating with Consultant respiratory Physicians (TICC-PCP) potentially reduced hospitalisations and emergency department (ED) visits, while increasing appropriate prescribing (e.g. steroids and antibiotics for exacerbations) and de-prescribing medicines associated with adverse drug reactions[14].

To date, 19 RCTs (none of which were pilot RCTs) have described healthcare professional interventions for people with COPD[15]. Recruitment processes, patient characteristics relating to

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comorbidities, prescribed medications and symptom scores were not described with the exception of one study. Other than Health-Related Quality of Life (HRQoL), objective and subjective health measures were not described. None of the interventions involved home-based visits and the majority focused on improving COPD treatment, medication adherence and / or inhaler technique. While evidence suggests such interventions may reduce risk of hospital admission, they have not been preceded by pilot studies nor shown a clear effect on HRQoL and have not involved delivery by Pharmacist IPs[15]. The longer-term clinical and cost effectiveness of Pharmacy professionals or other healthcare professional interventions for people with COPD is unclear.

We hypothesised that a RCT of a year-long complex TICC-PCP Intervention can attain RCT progression criteria and improve secondary (clinical) outcomes.

METHODS

Study design

We conducted a pragmatic, parallel group, pre-registered multicentre pilot RCT, in Greater Glasgow and Clyde and Lothian Health Boards (Scotland, UK), in accordance with the protocol[15] and the UK National Research Governance Framework[16]. With institutional review board approval from South East Scotland Research Ethics Committee (REC: 20/SS/0093), this report adheres to the Consort statement[17].

Adults with: COPD (Forced Expiratory Volume $(FEV)_1$/Forced Vital Capacity) < 0.7) and FEV_1 < 80% predicted; modified Medical Research Council (mMRC) dyspnoea scale ≥2[18]; and living at home were eligible to participate. Participants with lung or other malignancy were excluded. Participants were identified from respiratory out-patient clinics by consultant respiratory physicians in two hospitals who applied the exclusion criteria to their own clinic lists. Participants did not have an opportunity to self-refer into the trial. Researchers posted information and consent packs to participants then sent a reminder if no response had been received within two months. After four months, due to lower than expected responses, respiratory physicians passed recruitment packs to eligible participants. In passing recruitment packs to participants, the consultants did not spend time explaining the study or expecting the participants to read and agree to consent. Packs were passed to eligible participants at the end of a clinic, and participants asked to respond to the research team. Researchers phoned participants if no response had been received within one month. On obtaining informed consent in the post, researchers arranged home visits for baseline data collection (Supplementary appendix 1)[15]. Prescribing and service utilisation data were collected from health care records.

Randomisation and blinding

Immediately after baseline visits, participants were randomly allocated to TICC-PCP plus Usual Care (UC: National Health Service (NHS)), or UC alone (1:1 by a telephone- Interactive Voice Response System) using permuted blocks, stratified by recruitment centre and number of respiratory hospitalisations 12 months prior to recruitment (0 versus ≥1). The nature of the Intervention meant participant blinding was impossible although researchers were blinded to Intervention assignment.

TICC-PCP

TICC-PCP aimed to improve the management of COPD and comorbidities. One part-time NHS Pharmacist IP in each setting aimed to offer participants at least nine home based medication reviews[15] (monthly for six months, then bi-monthly for 6 months https://doi.org/10.1186/ISRCTN43508703), but worked flexibly, responding to participants' needs. Additional visits or phone calls were encouraged, in response to participants' needs, as assessed and agreed by the pharmacist. One named respiratory physician in each setting was available to each pharmacist for advice and support, fortnightly.

During home reviews, pharmacists assessed respiratory and other health problems, referred to local clinical guidelines when autonomously initiating, modifying or deprescribing treatments and addressed broader health determinants e.g. through social prescribing (referral to community services with the aim of improving health)[19]. Pharmacists co-ordinated all actions with existing primary care e.g. GP teams, and secondary care teams, remotely recording actions on clinical systems. A protocol paper provides further details[15].

Outcomes

The primary outcome was achievement of four, definitive RCT-based progression criteria:

1. Recruitment of ≥70% of invited participants within four months;
2. ≥70% of Intervention arm participants receiving TICC-PCP as planned (nine visits, at least monthly for six months then every two months) excluding those who died or developed incapacity);
3. ≥80% of participants (excluding those who died or developed incapacity) remaining until 21-month data collection;
4. ≥90% of in-person data collected at each study time point excluding those who died or developed incapacity.

The percentage of missing data was calculated as: number of missing expected data points divided by the total number of expected data points, multiplied by 100. Blood results and a modified version of the Patient Experience with Treatment and Self-management (PETS: a patient-reported measure of treatment burden which has not been validated)[20], were excluded.

Secondary outcomes (in each of TICC-PCP plus UC and UC alone during follow up) were: primary care contacts; prescribed medicines for: respiratory conditions; bone health; gastrointestinal problems; pain; cardiovascular disorders; depression; anxiety; anaemia; and vitamin or other dietary insufficiency. Also, ED attendances and hospital admissions for respiratory and non-respiratory reasons; out-patient attendances; death; COPD exacerbations (confirmed by patient report on use of rescue pack (steroids and/or antibiotics); HRQoL using EQ-5D-5L[21]; mMRC; COPD Assessment Test (CAT)[22]; falls and fractures; PETS; Patient Health Questionnaire-4 Item (PHQ-4) depression and anxiety score and sub-scores[23].

Sample size

Based on our feasibility study[14], we aimed to invite 160 eligible participants, to recruit approximately 100, to allow estimation of the percentage consenting with a precision of ±7.5%[24].

Statistical methods

Counts and percentages were used for categorical data, means and standard deviations, or medians and Interquartile Range for continuous data depending on the distribution. For primary care and acute healthcare contacts during follow-up, event rates per 100 person-years were reported, calculated as the total number of events divided by the total person-years of observation across all participants. Baseline data were summarised for all randomised participants. Participants were censored (no further data collected) if they died or lost capacity. If the study Steering group decided to withdraw a participant from attending further study visits (e.g. because of rapidly worsening health status or development of a malignancy), the participant received no further face to face

contact but the participant's medical records could still be accessed by the study team. All outputs were provided using R Studio and R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Pilot studies are not powered to provide conclusive evidence of effectiveness[24] therefore the Statistical Analysis Plan (Supplementary appendix 2) includes no formal testing of hypotheses, comparisons between groups, interim analyses or stopping guidelines. Given this was a pilot study, there was no formal requirement for a power calculation taking account of losses to follow up (for whatever reason e.g. death or loss of capacity), but this study does provide us with the information on loss to follow-up which will be utilised when obtaining a sample size calculation for a definitive study. The qualitative process evaluation is described separately[25] and an economic evaluation will be published subsequently.

Patient and public involvement

Patients and the public were involved in the study design and writing patient invitation packs.

RESULTS

Primary outcome

Recruitment. Between 7th July 2021 and 7th November 2021, researchers posted invitations to 100 eligible participants and 52 consented. However, 19 posted invitations were not received due to a postal strike, and two people died before receiving an invitation, giving a recruitment rate of 52/79 (65.8%). In the following two months, consultant respiratory physicians passed study information to 65 additional participants. Fifty-eight (58/65 (89.2%)) provided signed consent, giving 110/144 (76%) recruitment over six months (Fig. 1).

TICC-PCP intervention delivery. Of 55 participants assigned to the Intervention arm, one was immediately withdrawn by the steering group because of acute deterioration and another died prior to the first intervention visit.

Table 1 shows fewer than expected (13/49 (27%) of participants who did not die or develop incapacity by 12 months, received the intervention as planned (at least six contacts within six months and at least three contacts in the subsequent six months). These 13 participants received a higher than expected median number of contacts (16 (13, 17). During the first six months, 33/51(65%) received at least six contacts, with a median of 9 (7, 11) per participant. Table 1 shows all 53 remaining participants received at least one home visit with a median of 9 (7, 12) contacts per participant (the majority were home visits) median duration 27.1 (23.3, 37.5) minutes per contact. Home visits lasted a median of 20.6 (17.9, 31.9) minutes and phone calls 5.6 (3.8, 8.0) minutes).

Table 1 also describes pharmacists' interventions: 14/52 (26.9%) received new diagnoses: Osteoporosis (n = 4); Depression (n = 3); Hypertension (n = 3); Angina (n = 2); Left Ventricular Systolic Dysfunction (n = 2); and 28/52 (52.8%) received inhaler technique guidance. A minority 6/53 (11.3%) received social prescribing referrals: local walking groups (n = 3) and exercise classes in local gyms (n = 3). All intervention arm participants were referred to their GP for various reasons e.g. escalating chest pain, further assessment for treatment resistant depression. Forty five (45/53 (84.9%) were referred to respiratory consultants for reasons including: advanced assessment and care for escalating respiratory symptoms, palliation and prescribing of benzodiazepines, oxygen assessment and initiation. Twenty five (25/53 (47.2%) to other respiratory services e.g. respiratory teams and 16/53 (30.2%) for bone densitometry. Three (3/53 (5.7%) participants had an ambulance called by the pharmacist due to acute respiratory deterioration during visits.

Data collection. Table 2 shows the median percentage of data collected in-person across all eight (three monthly) researcher visits was 89.5 (72.9, 92.3).

Retention. Figure 1 shows 25 participants died (14 Intervention, 11 UC) and one participant lost capacity during the 21 month follow-up. No participants voluntarily withdrew from the trial. Excluding the 26 participants who died or developed incapacity, 79/84 (94%) participants had data collected at 21 month follow-up. Five participants were withdrawn from attending study visits by the study Steering Group (n = 1 Intervention; n = 4 UC [n = 1 carer's burden; n = 1 too unwell, n = 2 no longer interested]) but data was obtained by the study team via their clinical records up to the 21 month follow-up. Of the 79 participants who were eligible to attend the 21 month follow-up visit, 74 (94%) attended the visit as planned (Fig. 1).

Baseline demographic and clinical characteristics. Of those randomised, Table 3 shows participants were mostly female (65/110 (59.1%), 109/110 (99.1%) white ethnicity, with a mean age 67.4 (SD 8.2) years. Most (109/110 (99.1%) were either current (36/110 (32.7%)) or previous (73/100 (66.4%)) smokers, having started smoking aged 15.2 (SD 4.7) years on average. Almost one third (29.1%) reported no daily exercise and mean Body Mass Index (25.5 kg/m^2) was in the 'overweight' category, with the majority having unintentionally lost weight in the past year. Modified MRC and CAT results confirmed the worst possible respiratory symptoms. The mean health state utility score of participants was 0.35 (SD 0.35). Perfect health (a utility score of 1) was reported by 3/110 (4%) of participants: 22/110 (21%) reported utility scores < 0 ("worse than death", as a utility score of 0 represents death). Participants had an average of 2.8 (SD 1.4) respiratory diagnoses and 11.5 (SD 6.9) morbidities comprising physical (10.4 (SD 6.4)) and mental health co-morbidities (1.1 (SD 1.4)).

Participants had an average of 16.9 (SD 12.9) primary care contacts, accounting for 50% of the total number of healthcare contacts; most were with GPs, followed by COPD specialist teams and practice Nurses.

Nineteen (17.3%) participants had at least one ED visit: mean 1.5 (SD 0.8): 13/110 (11.8%) had presentations for respiratory reasons and 9/110 (8.2%) for non-respiratory reasons. Forty-nine (44.5%) participants had at least one hospital admission in the previous 12 months, average 2.2 (SD 1.7) per participant, mostly for respiratory causes (44/110 (40.0%)). A majority (100/110 (90.9%)) had attended multiple out-patient appointments.

Participants had 11.5 (SD 5.0) daily prescribed medicines (including oxygen). Medicine types included 37/110 (33.6%) receiving Calcium and/or Vitamin D, and 37/110 (33.6%) receiving Anticholinergic and/or sedative medicines increasing falls risk e.g. antidepressants; antihistamines; and anxiolytics.

Participants felt that the work associated with COPD self-management was not as burdensome as the impact of the work on their health and wellbeing (Table 4).

Baseline costs. The mean cost (healthcare contacts and medicines) for the year prior to baseline was £7,254.30 (SD: £8,654.41) (Fig. 2). Figure 2 also shows at baseline, participants had ten fold higher numbers of secondary care contacts.

Secondary outcomes (follow up)

At study closure, there were 25 deaths (14 Intervention (6 respiratory, 3 non respiratory and 5 unknown cause) and 11 UC (3 respiratory, 4 non-respiratory and 4 unknown cause)) (Fig. 1). The mean time to death in the Intervention arm was 356.5 days (SD 194.4) and 227.2 (SD 159.2) in UC. Figure 1 shows numbers censored (with reasons) after randomisation. There were censored participants at each follow up point, starting from 3 month follow

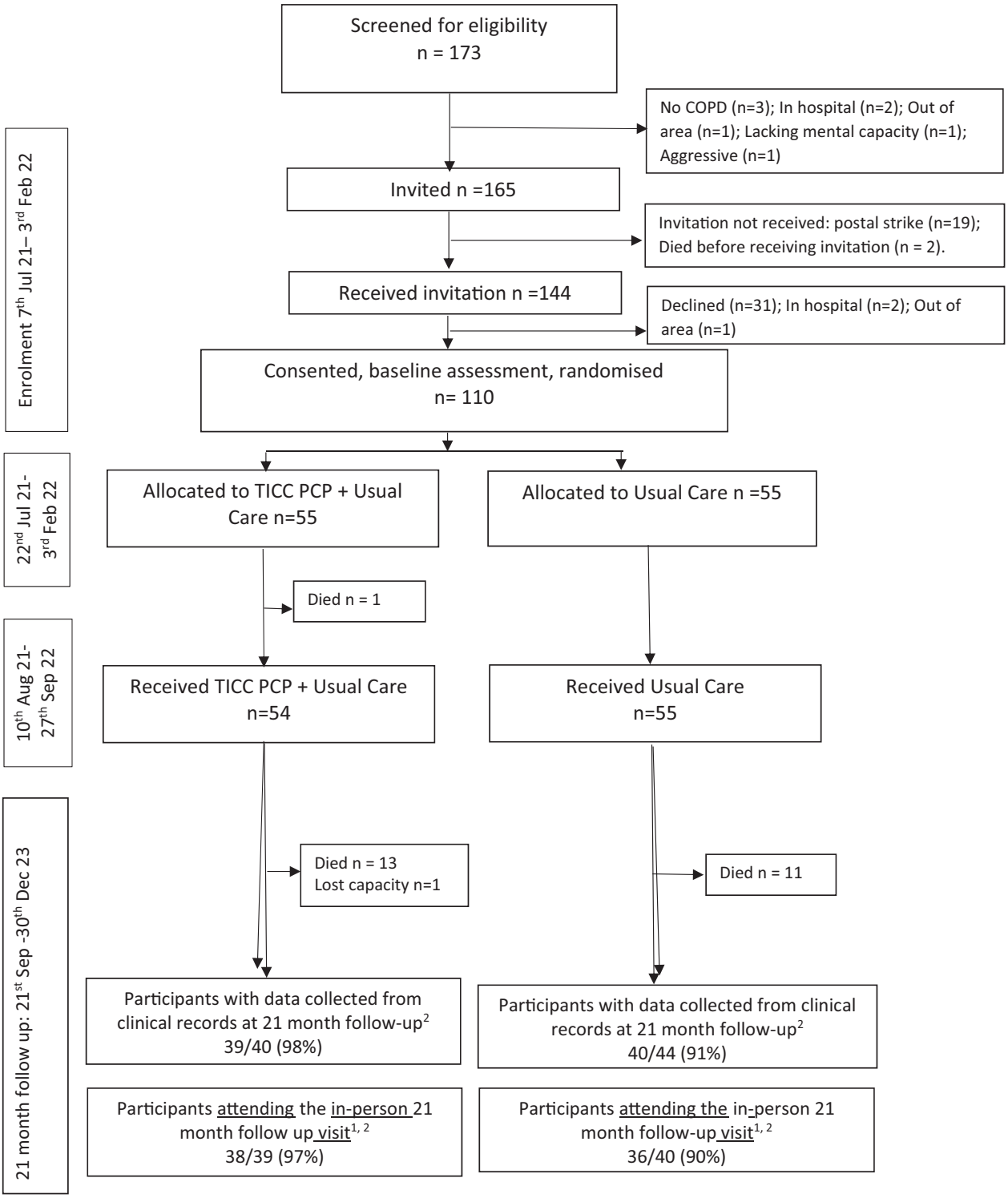

Fig. 1 Participant flow. [1]Participant withdrawn from attending study visits in the 'TICC PCP + Usual Care' group prior to receiving intervention. 4 participants withdrawn from attending study visits in the 'Usual Care' group (2 no longer interested; 1 too unwell; 1 with carer's burden) following usual care but prior to 21 month follow up. Data for participants withdrawn from attending study visits was still collected from clinical records up until 21 month follow up. [2]Excluding those who died or lost capacity prior to 21 month follow up.

up. This explains why follow up results (Tables 5–8), did not include all 110 participants.

All secondary outcomes were collected at six pre-specified timepoints (3, 6, 9, 12, 18 and 21 months); only 12 and 21 month-data are shown in Tables 5 to 8, for simplicity.

Prescribed medicines. Table 5 shows differences in the percentage of participants prescribed medicines. From baseline to 21 months, the average number of prescribed medicines increased in both arms. More participants in the intervention arm were prescribed medicines for: bone strengthening;

Table 1. Intervention delivery.

Variable	Summary Statistic	Intervention Group (N = 55)
At least 70% of intervention group participants receiving the intervention as planned (at least monthly for 6 months then every two months for one year) from the start of the randomisation.		
Had at least 6 contacts within 6 months of randomisation AND had at least 3 contacts between 6–12 months after randomisation (of those who did not die or develop incapacity by 12 months)	N (Nmissing) N (%) Yes N (%) No	49[a] (0) 13 (26.5%) 36 (73.5%)
Number of contacts (for those who had at least 6 contacts within 6 months of randomisation AND had at least 3 contacts between 6–12 months after randomisation	N (Nmissing) Median (IQR)	13 (0) 16.0 (13.0, 17.0)
Had at least 6 contacts within six months of randomisation (of those who did not die or develop incapacity by six months)	N (Nmissing) N (%) Yes N (%) No	51[b] (0) 33 (64.7%) 18 (35.3%)
Number of contacts (for those who had at least 6 contacts within six months of randomisation)	N (Nmissing) Median (IQR)	33 (0) 9.0 (7.0, 11.0)
Had at least one contact (face-to-face or via telephone/email)	N (Nmissing) N (%) Yes N (%) No	55 (0) 53 (96.4%) 2 (3.6%)
Total number of contacts (face-to-face or via telephone/email)	N (Nmissing) Median (IQR)	53 (0) 9.0 (7.0, 12.0)
Average contact duration, in minutes (face-to-face or via telephone/email)	N (Nmissing) Median (IQR)	53 (0) 27.1 (23.3, 37.5)
Average face-to-face contact duration, in minutes	N (Nmissing) Median (IQR)	53 (0) 20.6 (17.9, 31.9)
Average telephone/email contact duration, in minutes	N (Nmissing) Median (IQR)	47 (0) 5.6 (3.8, 8.0)
Interventions made by pharmacists	**Summary Statistic**	**N = 53**
New diagnosis made by pharmacist	N (Nmissing) N (%) Yes	52 (1) 14 (26.9%)
Inhaler technique assessment **or** advice	N (Nmissing) N (%) Yes	53 (0) 42 (79.2%)
Inhaler technique assessment **and** advice	N (Nmissing) N (%) Yes	53 (0) 28 (52.8%)
Other advice e.g. exacerbations, oedema, rescue packs, falls	N (Nmissing) N (%) Yes	53 (0) 52 (98.1%)
Self-management plan	N (Nmissing) N (%) Yes	53 (0) 47 (88.7%)
Mental health review / discussion	N (Nmissing) N (%) Yes	53 (0) 37 (69.8%)
Medicines advice given	N (Nmissing) N (%) Yes	53 (0) 53 (100.0%)
Social prescribing[c] (includes any of the following: CAB/ Foodbank/Benefits/Housing/ Local support groups)	N (Nmissing) N (%) Yes	53 (0) 6 (11.3%)
Social prescribing[c] – number of the following: CAB/ Foodbank/Benefits/ Housing/ Local support groups	N (Nmissing) Median (IQR)	6 (0) 2.0 (2.0, 2.8)
Referred to GP	N (Nmissing) N (%) Yes	53 (0) 53 (100.0%)
Number of issues referred to the GP for (e.g. to start/stop a medication, for a referral, take bloods, etc.)	N (Nmissing) Median (IQR)	53 (0) 8.0 (5.0, 11.0)
Referred to a respiratory consultant	N (Nmissing) N (%) Yes	53 (0) 45 (84.9%)
Number of issues referred to the consultant for (e.g. X-ray results, etc.)	N (Nmissing) Median (IQR)	45 (0) 3.0 (2.0, 5.0)
Informing practice or community pharmacist of prescription issue (e.g. request for dosette box, delivery of medication, change to prescription)	N (Nmissing) N (%) Yes	53 (0) 13 (24.5%)
Referral to other respiratory services (e.g. respiratory nurse, REACT, Pulmonary rehabilitation, NRT referral, MDU, etc.)	N (Nmissing) N (%) Yes	53 (0) 25 (47.2%)
Number of referrals to other respiratory services (e.g. respiratory nurse)	N (Nmissing) Median (IQR)	25 (0) 2.0 (1.0, 2.0)
Occupational therapist or physiotherapist referral	N (Nmissing) N (%) Yes	53 (0) 20 (37.7%)
Number of referrals to occupational therapist or physiotherapist	N (Nmissing) Median (IQR)	20 (0) 1.0 (1.0, 3.0)
DEXA referral	N (Nmissing) N (%) Yes	53 (0) 16 (30.2%)
Any of the following performed: Nebuliser / Chest X-ray / ECG / CT / PSA / 6-min walk assessment	N (Nmissing) N (%) Yes	24 (29) 8 (33.3%)
Number of the following performed: Nebuliser / Chest X-ray / ECG / CT / PSA /6-min walk assessment	N (Nmissing) Median (IQR)	8 (29) 1.0 (1.0, 2.0)
Dietician referral	N (Nmissing) N (%) Yes	53 (0) 8 (15.1%)
Oxygen assessment referral	N (Nmissing) N (%) Yes	53 (0) 1 (1.9%)
Referral to one or more of the following: Community Respiratory Team, Mental Health Team, District Nurse, MDU	N (Nmissing) N (%) Yes	53 (0) 11 (20.8%)
Number of referrals to the following: Community Respiratory Team, Mental Health Team, District Nurse, MDU	N (Nmissing) Median (IQR)	11 (0) 1.0 (1.0, 1.5)
GP referral leading to GP calling an ambulance	N (Nmissing) N (%) Yes	53 (0) 3 (5.7%)
Ambulance call made during pharmacist visit	N (Nmissing) N (%) Yes	53 (0) 3 (5.7%)
Other appointments made	N (Nmissing) N (%) Yes	53 (0) 26 (49.1%)
Number of other appointments made	N (Nmissing) Median (IQR)	26 (0) 2.0 (1.0, 3.0)
Checked pedal pulses	N (Nmissing) N (%) Yes	25 (28) 1 (4.0%)
Diagnostics taken (e.g. temperature, weight, SpO_2, RR, CAT score, MRC)	N (Nmissing) N (%) Yes	53 (0) 53 (100.0%)
Observations and visual examination (oedema, colour, cyanosis, talk in full sentence)	N (Nmissing) N (%) Yes	53 (0) 52 (98.1%)
Auscultation performed	N (Nmissing) N (%) Yes	53 (0) 24 (45.3%)

[a]Six participants either died or lost capacity within 12 months of randomization.
[b]Four participants either died or lost capacity within 6 months of randomization.
[c]Referral to community services with the aim of improving health.

gastrointestinal; vitamin and other dietary insufficiencies, and fewer were prescribed medicines for pain, depression, and anxiety.

Acute healthcare utilisation. Overall, Table 6 results suggest a signal that participants in the intervention arm had fewer emergency department attendances and hospital admissions for respiratory reasons at 12 months (the end of the intervention period) as compared to participants in the UC arm, but any difference was attenuated at 21 months. Of note, the mean duration of admission for respiratory reasons at 12 months in the intervention arm was almost double the duration for participants in the UC arm. This pattern was similar for non-respiratory reasons.

Table 2. Data Collection and participant retention at follow up.

Variable	Summary Statistic	N = 84
Average percentage of in-person data collected across all visits (of those who did not die or develop incapacity by 21 month visit)	N (Nmissing)	84 (0)
	Median (IQR)	89.5 (72.9, 92.3)
At least 80% of ITT participants (excluding those who died or developed incapacity before the end of the study) remaining in the study until 21 month data collection		
Remained in study until 21 month visit (of those who did not die or develop incapacity by 21 month visit)	N (Nmissing)	84 (0)
	N (%) Yes	74 (88.0%)

Primary care contacts showed few differences between Intervention and UC (Table 7).

A proxy for COPD exacerbations involved researchers visiting participants and counting used 'rescue packs' (short course oral prednisolone and/or antibiotics) three monthly (Table 7). By 12 months, a baseline imbalance was attenuated and there was a signal that the mean number of rescue packs used by intervention arm participants was lower than in UC participants.

HRQoL was assessed during in person visits by researchers (Table 8). Self-rated overall health scores appeared higher across all time points, in the intervention arm. In both study arms at each follow up point compared with baseline, the proportion of participants with utility index scores less than zero decreased, suggesting a possible positive effect from repeated researcher visits. Comparing intervention versus UC, there did not appear to be any signal of improvement (reduction) in self-reported falls (Table 8) across all follow up points.

Table 8 also suggests that at 12 months, PETS scores were lower (suggesting the workload and impact of treatment became less of a burden) and PHQ-4 average scores were lower (participants reported less anxiety and depression) in the intervention arm.

DISCUSSION

Statement of principal findings

Recruitment, retention, and data collection targets were achieved as planned (or with slight modifications). One quarter of TICC-PCP intervention participants received at least the planned monthly (first six months) then bi-monthly (subsequent six months) contacts: they received almost double the expected number of home visits. The remainder received nine contacts, on average, suggesting the flexibility of TICC-PCP visits led to tailoring by Pharmacists according to participants' needs.

A multimorbid cohort (mean of 11.5 (SD 6.9) conditions at baseline) received an increasing number of daily medicines over time.

Pharmacists built trusting therapeutic relationships, overcoming challenges to in-person contact during the COVID-19 pandemic. They conducted clinical assessments and prescribed a range of medicines in collaboration with consultant respiratory physicians and wider teams. Intervention arm participants appeared less likely to use rescue packs for exacerbations and attend emergency care or hospital for respiratory reasons although the duration of hospitalisation (for any reason) was longer for intervention arm participants. This latter observation appears at odds with the rest of the findings and requires further exploration in a definitive trial. A signal of longer duration of hospitalisations suggests participants admitted to hospital from the intervention arm were sicker than participants in the UC arm. The optimal time to detect any apparent improvement in outcomes appeared to be 12 months (end of intervention), which has implications for designing a subsequent definitive trial.

There were signs that health related quality of life, anxiety and depression and treatment burden outcomes favoured the intervention arm as compared with the UC arm during the one year intervention, without any apparent increase in primary care GP contacts.

The need for a subsequent definitive trial is supported by a parallel qualitative process evaluation in which participants (particularly those living in more socioeconomically deprived areas) and staff were supportive of the TICC-PCP approach[25]. In such a trial, if the primary outcome is the number of participants with Emergency Department attendance at 12 months and we observe a proportion attending the Emergency Department in UC of 0.325, and the proportional improvement in TICC-PCP vs UC was 0.125, the estimated sample size per arm with data would be 208 with 80% power.

Strengths and weaknesses

Strengths included detailed participant and service utilisation data, recruitment and follow up processes, a reasonable period of follow up, good description of the intervention and detailed changes made by pharmacists. Unlike previous studies of this type[26–28], where Pharmacists with additional respiratory therapeutics training delivered care in clinics, focusing on the single morbidity of respiratory disease, offering support for inhaler technique and advice on swift management of exacerbations, the TICC-PCP pharmacists were generalists. Given that most pharmacists are generalists, we suggest this is likely to aid implementation, while helping to address co-morbidities, many of which worsen quality of life in patients with COPD.

The collaborative, integrated intervention involving consultant respiratory physicians ensured safe practice and clinical governance.

Weaknesses included uncertainty on the typology of participants most likely to benefit from TICC-PCP, and, while the majority of participants lived in the most socioeconomically deprived Scottish areas, there was a noted lack of ethnic diversity. In a future RCT, consideration can be given to modifying recruitment to increase uptake in minority ethnic groups and people who struggle to attend out patient appointments e.g. people experiencing homelessness. Subgroup analyses could identify those who experience greatest gain.

Uncertainty as to the magnitude of the positive Hawthorne effect of three monthly home visits by researchers could be overcome if outcome data were collected through remote record linkage. This approach may also facilitate identification of cause of death. Enrolment and the first four months of TICC PCP delivery also overlapped with COVID-19 lockdown when much community based research was paused, however our trial steering group made the decision to continue the study, with researchers donning and doffing protective clothing and equipment, given the potential benefits of home visits to otherwise isolated, housebound participants.

Interpretation in context of published literature

RCTs of HCP-led interventions for people with COPD focused on specific respiratory issues e.g. medicine adherence/inhaler technique, rather than addressing comorbidities and wider health

Table 3. Baseline demographic, clinical and healthcare utilisation (N (0 missing) for 110 randomised, unless otherwise stated).

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Age (years)	Mean (SD)	67.4 (8.2)	68.2 (8.2)	66.6 (8.2)
Gender	N (%) Male	45 (40.9%)	25 (45.5%)	20 (36.4%)
	N (%) Female	65 (59.1%)	30 (54.5%)	35 (63.6%)
Ethnicity	N (%) White	109 (99.1%)	55 (100.0%)	54 (98.2%)
	N (%) Other	1 (0.9%)	0 (0.0%)	1 (1.8%)
Receiving any benefits	N (%) Yes	77 (70.0%)	39 (70.9%)	38 (69.1%)
	N (%) No	33 (30.0%)	16 (29.1%)	17 (30.9%)
SIMD Quintile	N (Nmissing)	109 (1)	54 (1)	55 (0)
	N (%) 1 - Most Deprived	42 (38.5%)	15 (27.8%)	27 (49.1%)
	N (%) 2N (%) 3N (%) 4N (%) 5 - Least Deprived	27 (24.8%)	18 (33.3%)	9 (16.4%)
		17 (15.6%)	12 (22.2%)	5 (9.1%)
		10 (9.2%)	3 (5.6%)	7 (12.7%)
		13 (11.9%)	6 (11.1%)	7 (12.7%)
Smoking status	N (%) Current smoker	36 (32.7%)	20 (36.4%)	16 (29.1%)
	N (%) Former smoker	73 (66.4%)	35 (63.6%)	38 (69.1%)
	N (%) Never	1 (0.9%)	0 (0.0%)	1 (1.8%)
Age started smoking (for current/former smokers)	N (Nmissing)	104 (5)	53 (2)	51 (3)
	Mean (SD)	15.2 (4.7)	14.8 (4.3)	15.5 (5.1)
Typical level of daily exercise	N (%) None	32 (29.1%)	15 (27.3%)	17 (30.9%)
	N (%) Low	62 (56.4%)	31 (56.4%)	31 (56.4%)
	N (%) Medium	15 (13.6%)	9 (16.4%)	6 (10.9%)
	N (%) High	1 (0.9%)	0 (0.0%)	1 (1.8%)
Current alcohol drinker	N (%) Yes	59 (53.6%)	32 (58.2%)	27 (49.1%)
	N (%) No	51 (46.4%)	23 (41.8%)	28 (50.9%)
Typical number of units consumed per day (for current drinkers)	N (Nmissing)	37 (22)	21 (11)	16 (11)
	Mean (SD)	6.6 (5.7)	6.5 (7.2)	6.8 (3.3)
BMI (kg/m^2)	N (Nmissing)	102 (8)	53 (2)	49 (6)
	Mean (SD)	25.5 (7.2)	24.4 (6.4)	26.7 (7.9)
SBP (mmHg)	N (Nmissing)	105 (5)	53 (2)	52 (3)
	Mean (SD)	139.9 (22.9)	137.5 (24.3)	142.3 (21.5)
DBP (mmHg)	N (Nmissing)	105 (5)	53 (2)	52 (3)
	Mean (SD)	83.6 (14.0)	80.5 (12.5)	86.8 (14.9)
Oxygen saturation (%)	N (Nmissing)	104 (6)	54 (1)	50 (5)
	Mean (SD)	94.4 (3.2)	94.5 (3.1)	94.3 (3.3)
On Oxygen	N (%) Yes	23 (20.9%)	11 (20.0%)	12 (21.8%)
	N (%) No	87 (79.1%)	44 (80.0%)	43 (78.2%)
Modified MRC score	Mean (SD)	3.2 (0.9)	3.2 (1.0)	3.1 (0.9)
COPD Assessment Test	Mean (SD)	27.1 (7.8)	26.4 (8.2)	27.8 (7.5)
Health Related Quality of Life Utility Index score (min = 0.59 worst health, max = 1 best health)	N (Nmissing)	106 (4)	53 (2)	53 (2)
	Mean (SD)	0.35 (0.35)	0.36 (0.36)	0.35 (0.35)
Utility Index score <0	N (Nmissing)	106 (4)	53 (2)	53 (2)
	N (%) Yes	22 (20.8%)	10 (18.9%)	12 (22.6%)
On a scale from 0 (worst health) to 100 (best health) rate how your health is today	N (Nmissing)	109 (1)	54 (1)	55 (0)
	Mean (SD)	57.9 (20.2)	57.9 (20.7)	57.8 (19.8)
Diagnoses				
Number of respiratory diagnoses	Mean (SD)	2.8 (1.4)	2.8 (1.4)	2.8 (1.5)
Number of non-respiratory diagnoses	Mean (SD)	7.6 (5.8)	7.5 (5.5)	7.8 (6.1)
Physical morbidities (respiratory / other)	Mean (SD)	10.4 (6.4)	10.3 (6.1)	10.6 (6.8)
Mental health diagnoses	Mean (SD)	1.1 (1.4)	1.0 (1.4)	1.2 (1.5)
PHQ-4 total score (range 0 = best to 6 = worst health)	N (Nmissing)	105 (5)	53 (2)	52 (3)
	Mean (SD)	5.0 (3.8)	5.1 (3.9)	4.8 (3.8)
COPD exacerbations				
Self-management plan / rescue pack in house	N (%) Yes	51 (46.4%)	29 (52.7%)	22 (40.0%)
Number of rescue packs used in past 12 months	N (Nmissing)	51 (0)	29 (0)	22 (0)
	Mean (SD)	3.9 (3.8)	4.5 (4.5)	3.1 (2.6)
Exacerbation (rescue pack) in past 12 months	N (Nmissing)	109 (1)	54 (1)	55 (0)
	N (%) More than 2 packs	63 (57.8%)	31 (57.4%)	32 (58.2%)
	N (%) 2 packs or less	46 (42.2%)	23 (42.6%)	23 (41.8%)

Table 3 continued

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Primary Care				
Any primary care contact	N (%) Yes	107 (97.3%)	55 (100%)	52 (94.5%)
Number of primary care contacts	N (Nmissing) Mean (SD)	107 (0) 16.9 (12.9)	55 (0) 17.5 (13.8)	52 (0) 16.3 (12.1)
COPD Specialist Team	N (%) Yes	53 (48.2%)	30 (54.5%)	23 (41.8%)
Total number of COPD Specialist Team contacts	N (Nmissing) Mean (SD)	53 (0) 4.5 (5.9)	30 (0) 5.3 (7.4)	23 (0) 3.3 (3.0)
A&E				
Any visit	N (%) Yes	19 (17.3%)	9 (16.4%)	10 (18.2%)
Total number of visits	N (Nmissing) Mean (SD)	19 (0) 1.5 (0.8)	9 (0) 1.6 (0.7)	10 (0) 1.5 (1.0)
Respiratory cause	N (%) Yes	13 (11.8%)	6 (10.9%)	7 (12.7%)
Non-respiratory cause	N (%) Yes	9 (8.2%)	5 (9.1%)	4 (7.3%)
Hospital Admission				
Any admission	N (%) Yes	49 (44.5%)	26 (47.3%)	23 (41.8%)
Number of admissions	N (Nmissing) Mean (SD)	49 (0) 2.2 (1.7)	26 (0) 1.9 (1.1)	23 (0) 2.6 (2.1)
Any admission (respiratory cause)	N (%) Yes	44 (40.0%)	24 (43.6%)	20 (36.4%)
Any admission (non-respiratory)	N (%) Yes	13 (11.8%)	7 (12.7%)	6 (10.9%)
Outpatient Appointments				
Any attended appointment	N (%) Yes	100 (90.9%)	52 (94.5%)	48 (87.3%)
Number of appointments attended	N (Nmissing) Mean (SD)	100 (0) 5.7 (5.2)	52 (0) 6.0 (5.4)	48 (0) 5.4 (5.1)
Prescribed medicines				
Number of medicines	Mean (SD)	11.5 (5.0)	11.5 (4.8)	11.6 (5.2)
Flu vaccine	N (Nmissing) N (%) Yes	107 (3) 100 (93.5%)	54 (1) 53 (98.1%)	53 (2) 47 (88.7%)
COVID vaccinated	N (%) Yes	110 (100.0%)	55 (100.0%)	55 (100.0%)

Table 4. Baseline Patient Experience with Treatment & Self-Management (PETS) Questionnaire Standardised Scores.

Score	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Medical Information	N (Nmissing)	109 (1) 21 (0, 29)	55 (0) 25 (0, 27)	54 (1) 0 (0, 32)
Medicines		0 (0, 25)	0 (0, 25)	0 (0, 25)
Medicines reliance bother		0 (0, 75)	0 (0, 50)	25 (0, 75)
Medical Appointments	N (Nmissing)	103 (7) 25 (8, 36)	52 (3) 25 (7, 30)	51 (4) 25 (10, 42)
Monitoring Health	N (Nmissing)	109 (1) 0 (0, 25)	54 (1) 0 (0, 25)	55 (0) 0 (0, 25)
Exercise (where appropriate)	N (Nmissing)	38 (19) 58 (50, 67)	19 (10) 50 (46, 63)	19 (9) 58 (50, 67)
Medical Equipment	N (Nmissing)	107 (3) 0 (0, 17)	55 (0) 0 (0, 21)	52 (3) 0 (0, 10)
Relationships	N (Nmissing)	109 (1) 25 (0, 38)	55 (0) 25 (0, 38)	54 (1) 25 (6, 38)
Difficulty with Healthcare Services	N (Nmissing)	102 (8) 39 (33, 50)	50 (5) 39 (33, 49)	52 (3) 38 (33, 50)
Role and Social Activity Limitations		20 (10, 49)	20 (15, 50)	20 (10, 43)
Physical and Mental Exhaustion		50 (25, 70)	45 (20, 60)	55 (40, 80)
Workload Summary Index	N (Nmissing)	101 (9) 14 (4, 31)	51 (4) 14 (6, 26)	50 (5) 13 (3, 32)
Impact Summary Index		38 (21, 54)	35 (19, 51)	43 (24, 55)

(0 = lowest burden; 100 = highest burden) (N (0 missing) for 110 randomised, 55 Intervention and 55 Usual Care, and Median (IQR) unless otherwise stated).

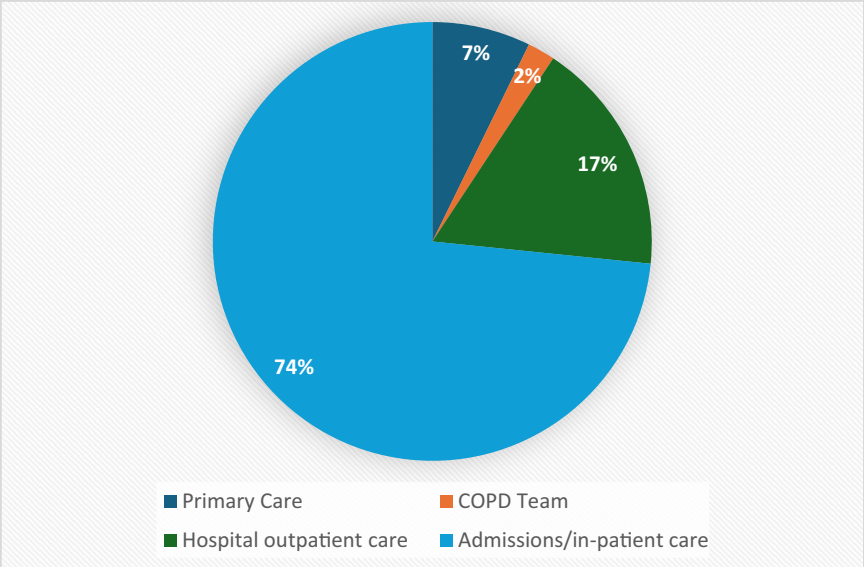

Fig. 2 Distribution of total healthcare contact costs 12 months prior to baseline by type of healthcare contact.

determinants[29–34]. Pharmacist prescriber led home visits remain untested in this and other therapeutic areas[29–34]. Definitive trials assessing outcome measures other than HRQoL are lacking[29–34]. Three systematic reviews (two focused specifically on pharmacist interventions/care) reported that the available evidence lacked robustness[26–28]. Two underscored the importance of monitoring and reporting variations in UC over time, as we have done[27,28]. The wider evidence base for pharmacist medication review in the UK is marked by two studies, both of which involved low intensity interventions, and neither of which showed improved outcomes[13,35]. In the HOOPS, pharmacists visited people with Left Ventricular Systolic Dysfunction (LVSD) in their homes or General Practices, conducting medicine reviews that were similar to those delivered by TICC-PCP pharmacists, although the latter prescribed autonomously while HOOPS pharmacists made recommendations to GPs for medicine changes. The HOOPS failed to reach the primary end point (death/hospitalisation for heart failure), despite improvements in the prescribing of evidence based disease modifying treatments for LVSD.

In the HOMER RCT, two home visits by pharmacists (non prescribers) to elderly patients receiving polypharmacy post discharge, was associated with a significantly higher rate of hospital admissions and did not improve quality of life. GP home visits increased, and there was a statistically insignificant increase in deaths in the control group[35]. While we did not observe the former, there were more deaths in the TICC-PCP arm.

Deprescribing interventions have been the focus of much research over the past 20 years, however, trials are generally of short duration (less than one year) and clinical and health service outcomes have not been comprehensively assessed[36]. As far as we are aware, IP Pharmacist led deprescribing has not been explored as a means of reducing falls or emergency department visits, and the impact on patients remains unclear.

Generalist Pharmacy technicians are capable of undertaking many of Pharmacists' traditional roles including some of those enacted by pharmacists in the TICC-PCP intervention, raising the question of whether pharmacy technicians could offer a more affordable approach[37].

Pharmacists commonly made clinical guideline based changes to medicines in one or more of the seven categories described in Table 5. There was no overall signal of Pharmacists having de-prescribed to a greater extent than UC (mean number of medicines increased in both groups) although deprescribing was observed in relation to medicines for anxiety and depression. Respiratory interventions were the most common, and possibly contributed to the pattern of fewer unscheduled care attendances. A subsequent definitive RCT is needed to test this hypothesis.

Home visits and protocol led changes to the defined range of medicines identified in this study could be undertaken by healthcare professionals with less advanced training than independent prescriber pharmacists. For example, Pharmacy Technicians could provide the relationship based pharmaceutical care valued by participants, while achieving similar outcomes at lower cost, enabling long-term sustainability. Such a trial could target people with COPD and co-morbidities who struggle to access primary care, e.g. people experiencing homelessness, who have a disease and treatment burden in excess of those shown by participants in the present study, and are less likely to receive medicines for COPD[12]. Alternatively, the target group could be people with higher rates of emergency healthcare use where COPD is among the principal causes, e.g. people using illicit opioids[38].

The observed improvements in HRQoL, anxiety, depression and treatment burden in the intervention arm relative to UC, were achieved despite signs that the intervention led to a decrease in medicines for anxiety and depression in the intervention arm relative to UC. It is possible that the frequent (nine visits over a year) healthcare professional home visits to people who are increasingly breathless at rest and housebound, provided reassurance while expediting access to consultant respiratory physician advice. Findings from the parallel qualitative process evaluation support the idea that the relational aspect of the visits were highly valued by participants who are increasingly co-morbid with limited mobility[25].

Baseline utility scores and health state utilities were lower than the values reported in other cross-country settings[39] and studies of other long-term conditions[40]. Reasons for this are unclear, but the extent of socioeconomic disadvantage and number of comorbidities may be contributory[41].

Table 5. Prescribed medicines at follow up[a].

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Any medicines prescribed	N N (%) Baseline	110 (0) 110 (100.0%)	55 (0) 55 (100.0%)	55 (0) 55 (100.0%)
	N N (%) 12 months	91 (0) 91 (100.0%)	49 (0) 49 (100.0%)	42 (0) 42 (100.0%)
	N N (%) 21 months	109 (0) 109 (100.0%)	55 (0) 55 (100.0%)	54 (0) 54 (100.0%)
Number of medicines prescribed daily	Baseline N Mean (SD)	110 11.4 (4.9)	55 11.4 (4.8)	55 11.5 (5.1)
	12 months N Mean (SD)	91 14.6 (7.2)	49 14.9 (6.4)	42 14.2 (8.1)
	21 months N Mean (SD)	109 13.8 (5.5)	55 14.4 (5.5)	54 13.1 (5.5)
Any medicines prescribed for respiratory conditions	N N (%) Baseline	110 (0) 108 (98.2%)	55 (0) 54 (98.2%)	55 (0) 54 (98.2%)
	N N (%) 12 months	91 (19) 90 (98.9%)	49 (6) 48 (98.0%)	42 (13) 42 (100.0%)
	N N (%) 21 months	109 (1) 107 (98.2%)	55 (0) 54 (98.2%)	54 (1) 53 (98.1%)
Number of medicines for respiratory conditions	Baseline N Mean (SD)	108 3.5 (1.4)	54 3.6 (1.5)	54 3.5 (1.1)
	12 months N Mean (SD)	90 4.6 (1.8)	48 4.6 (1.6)	42 4.5 (2.0)
	21 months N Mean (SD)	107 4.5 (1.7)	54 4.6 (1.7)	53 4.4 (1.7)
Any medications prescribed for bone health	N N (%) Baseline	110 27 (24.5%)	55 14 (25.5%)	55 13 (23.6%)
	N N (%) 12 months	91 19 (20.9%)	49 16 (32.7%)	42 3 (7.1%)
	N N (%) 21 months	109 22 (20.2%)	55 14 (25.5%)	54 8 (14.8%)
Any medications prescribed for gastrointestinal problems	N N (%) Baseline	110 35 (31.8%)	55 16 (29.1%)	55 19 (34.5%)
	N N (%) 12 months	91 63 (69.2%)	49 36 (73.5%)	42 27 (64.3%)
	N N (%) 21 months	109 78 (71.6%)	55 42 (76.4%)	54 36 (66.7%)
Any medications prescribed for pain	N N (%) Baseline	110 47 (42.7%)	55 19 (34.5%)	55 28 (50.9%)
	N N (%)12 months	91 62 (68.1%)	49 31 (63.3%)	42 31 (73.8%)
	N N (%) 21 months	109 75 (68.8%)	55 39 (70.9%)	54 36 (66.7%)
Any medications prescribed for depression	N N (%) Baseline	110 29 (26.4%)	55 14 (25.5%)	55 15 (27.3%)
	N N (%) 12 months	91 35 (38.5%)	49 16 (32.7%)	42 19 (45.2%)
	N N (%) 21 months	109 38 (34.9%)	55 16 (29.1%)	54 22 (40.7%)
Any medications prescribed for anxiety	N N (%) Baseline	110 12 (10.9%)	55 6 (10.9%)	55 6 (10.9%)
	N N (%) 12 months	91 24 (26.4%)	49 11 (22.4%)	42 13 (31.0%)
	N N (%) 21 months	109 20 (18.3%)	55 9 (16.4%)	54 11 (20.4%)
Any medications for anaemia	N N (%) Baseline	110 (0) 0 (0.0%)	55 (0) 0 (0.0%)	55 (0) 0 (0.0%)
	N N (%) 12 months	91 (0) 26 (28.6%)	49 (0) 16 (32.7%)	42 (0) 10 (23.8%)
	N N (%) 21 months	109 (0) 29 (26.6%)	55 (0) 14 (25.5%)	54 (0) 15 (27.8%)
Any medications prescribed for a vitamin or other dietary insufficiency	N N (%) Baseline	110 25 (22.7%)	55 12 (21.8%)	55 13 (23.6%)
	N N (%) 12 months	91 54 (59.3%)	49 38 (77.6%)	42 16 (38.1%)
	N N (%) 21 months	109 55 (50.5%)	55 35 (63.6%)	54 20 (37.0%)

N medicines at baseline refer to number of medicines prescribed in the 12 months prior to baseline.
[a]no data missing at any time point for any variable.

Table 6. Follow up Acute Healthcare Utilisation.

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Respiratory outcomes				
Emergency Department attendance for respiratory reasons	N (Nmissing) N (%) At Baseline	110 (0) 13 (11.8%)	55 (0) 6 (10.9%)	55 (0) 7 (12.7%)
	N (Nmissing) N (%) 12 months	80 (30) 14 (17.5%)	44 (11) 6 (13.6%)	36 (19) 8 (22.2%)
	N (Nmissing) N (%) 21 months	68 (42) 8 (11.8%)	37 (18) 6 (16.2%)	31 (24) 2 (6.5%)
Number of Emergency Department attendances for respiratory reasons	Baseline N (Nmissing) Mean (SD) Event rate per 100 PY	13 (0) 1.4 (0.7) 16.36	6 (0) 1.2 (0.4) 12.73	7 (0) 1.6 (0.8) 20.00
	12 months N (Nmissing) Mean (SD) Event rate per 100 PY	14 (0) 1.6 (1.3) 21.52	6 (0) 1.7 (1.6) 18.28	8 (0) 1.6 (1.1) 24.91
	21 months N (Nmissing) Mean (SD) Event rate per 100 PY	8 (0) 1.1 (0.4) 14.22	6 (0) 1.0 (0.0) 18.21	2 (0) 1.5 (0.7) 9.89
Hospital admission for respiratory reasons	N (Nmissing) N (%) At Baseline	110 (0) 44 (40.0%)	55 (0) 24 (43.6%)	55 (0) 20 (36.4%)
	N (Nmissing) N (%) At 12 months	91 (19) 41 (45.1%)	47 (8) 16 (34.0%)	44 (11) 24 (54.5%)
	N (Nmissing) N (%) At 21 months	76 (34) 37 (48.7%)	42 (13) 18 (42.9%)	34 (21) 19 (55.9%)
Duration of Hospital Admissions for respiratory reasons (days)	Baseline N (Nmissing) Mean (SD)	36 (8) 12.2 (13.6)	19 (5) 11.5 (14.1)	17 (3) 13.1 (13.5)
	12 months N (Nmissing) Mean (SD)	41 (0) 14.6 (19.2)	16 (0) 21.2 (26.6)	24 (0) 10.3 (11.3)
	21 months N (Nmissing) Mean (SD)	37 (0) 13.9 (18.5)	18 (0) 16.6 (20.0)	19 (0) 11.4 (17.1)
Non-respiratory outcomes				
Emergency Department attendance for non-respiratory reasons	N (Nmissing) N (%) At Baseline	110 (0) 9 (8.2%)	55 (0) 5 (9.1%)	55 (0) 4 (7.3%)
	N (Nmissing) N (%) At 12 months	81 (29) 9 (11.1%)	43 (12) 4 (9.3%)	38 (17) 5 (13.2%)
	N (Nmissing) N (%) At 21 months	65 (45) 3 (4.6%)	35 (20) 1 (2.9%)	30 (25) 2 (6.7%)
Number of Emergency Department attendances for non-respiratory reasons	Baseline N (Nmissing) Mean (SD) Event rate per 100 PY	9 (0) 1.2 (0.4) 10.00	5 (0) 1.4 (0.5) 12.73	4 (0) 1.0 (0.0) 7.27
	12 months N (Nmissing) Mean (SD) Event rate per 100 PY	9 (0) 1.3 (0.5) 11.23	4 (0) 1.8 (0.5) 12.80	5 (0) 1.0 (0.0) 9.58
	21 months N (Nmissing) Mean (SD) Event rate per 100 PY	3 (0) 1.0 (0.0) 4.74	1 (0) 1.0 (-) 3.03	2 (0) 1.0 (0.0) 6.59
Hospital admission for non-respiratory reasons	N (Nmissing) N (%) At Baseline	110 (0) 13 (11.8%)	55 (0) 7 (12.7%)	55 (0) 6 (10.9%)
	N (Nmissing) N (%) At 12 months	87 (23) 22 (25.3%)	45 (10) 10 (22.2%)	42 (13) 12 (28.6%)
	N (Nmissing) N (%) At 21 months	65 (45) 13 (20.0%)	35 (20) 8 (22.9%)	30 (25) 5 (16.7%)

Table 6 continued

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Number of Hospital Admissions for non-respiratory reasons	Baseline N (Nmissing) Mean (SD) Event rate per 100 PY	13 (0) 1.2 (0.6) 13.64	7 (0) 1.0 (0.0) 12.73	6 (0) 1.3 (0.8) 14.55
	12 months N (Nmissing) Mean (SD) Event rate per 100 PY	22 (0) 1.5 (0.9) 29.94	10 (0) 1.7 (1.1) 31.08	12 (0) 1.2 (0.6) 28.75
	21 months N (Nmissing) Mean (SD) Event rate per 100 PY	13 (0) 1.2 (0.4) 25.27	8 (0) 1.2 (0.5) 30.34	5 (0) 1.2 (0.4) 19.77
Duration of Hospital Admissions since last visit for non-respiratory reasons (days)	Baseline N (Nmissing) Mean (SD)	5 (8) 11.6 (8.3)	2 (5) 7.5 (0.7)	3 (3) 14.3 (10.4)
	12 months N (Nmissing) Mean (SD)	22 (0) 14.7 (23.5)	10 (0) 23.2 (32.7)	12 (0) 7.7 (7.7)
	21 months N (Nmissing) Mean (SD)	13 (0) 6.4 (7.4)	8 (0) 7.2 (9.5)	5 (0) 5.0 (2.1)

N events at baseline refer to number of events in the 12 months prior to baseline. N (%) or Mean (SD).

Table 7. Follow up Primary Care Contacts and COPD exacerbations.

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Any Primary Care contact	N (Nmissing) N (%) At Baseline	110 (0) 107 (97.3%)	55 (0) 55 (100.0%)	55 (0) 52 (94.5%)
	N (Nmissing) N (%) At 12 months	103 (7) 100 (97.1%)	52 (3) 50 (96.2%)	51 (4) 50 (98.0%)
	N (Nmissing) N (%) At 21 months	81 (29) 77 (95.1%)	42 (13) 40 (95.2%)	39 (16) 37 (94.9%)
Number of Primary Care contacts	Baseline N (Nmissing) Mean (SD) Event rate per 100 PY	107 (0) 16.9 (12.9) 1646	55 (0) 17.5 (13.8) 1747	52 (0) 16.3 (12.1) 1545
	12 months N (Nmissing) Mean (SD) Event rate per 100 PY	100 (0) 15.1 (14.6) 1408	50 (0) 15.2 (11.8) 1391	50 (0) 14.9 (17.0) 1426
	21 months N (Nmissing) Mean (SD) Event rate per 100 PY	75 (2) 11.7 (10.9) 1389	39 (1) 11.8 (9.5) 1393	36 (1) 11.7 (12.3) 1384
COPD exacerbations[a]				
Baseline Visit Self-management plan / rescue pack in house	N (Nmissing) N (%) Yes	110 (0) 51 (46.4%)	55 (0) 29 (52.7%)	55 (0) 22 (40.0%)
Number of rescue packs used in past 12 months	N (Nmissing) Mean (SD)	51 (0) 3.9 (3.8)	29 (0) 4.5 (4.5)	22 (0) 3.1 (2.6)
12 Month Visit Self-management plan / rescue pack in house	N (Nmissing) N (%) Yes	78 (32) 56 (71.8%)	42 (13) 34 (81.0%)	36 (19) 22 (61.1%)
Number of rescue packs used	N (Nmissing) Mean (SD)	55 (1) 1.2 (1.1)	34 (0) 1.1 (0.9)	21 (1) 1.5 (1.3)
21 Month Visit Self-management plan / rescue pack in house	N (Nmissing) N (%) Yes	61 (49) 40 (65.6%)	33 (22) 28 (84.8%)	28 (27) 12 (42.9%)
Number of rescue packs used	N (Nmissing) Mean (SD)	40 (0) 1.4 (1.3)	28 (0) 1.2 (1.2)	12 (0) 1.8 (1.5)

N events at baseline refer to number of events in the 12 months prior to baseline. N (%) or Mean (SD).
[a]confirmed by patient report on use of rescue pack - steroids and/or antibiotics.

Table 8. Quality of Life, self-reported breathlessness, falls and patient experience of treatment.

Variable	Summary Statistic	All Randomised (N = 110)	Intervention (N = 55)	Usual Care (N = 55)
Utility index score (min = -0.59 worst; max = 1 best possible health)	**Baseline** N (Nmissing) Mean (SD)	106 (4) 0.352 (0.353)	53 (2) 0.356 (0.361)	53 (2) 0.348 (0.349)
	12 months N (Nmissing) Mean (SD)	70 (40) 0.517 (0.300)	38 (17) 0.550 (0.269)	32 (23) 0.479 (0.333)
	21 months N (Nmissing) Mean (SD)	57 (53) 0.528 (0.324)	29 (26) 0.555 (0.282)	28 (27) 0.500 (0.366)
COPD Assessment Test score (higher values correspond with increasing breathlessness)	**Baseline** N (Nmissing) Mean (SD)	110 (0) 27.1 (7.8)	55 (0) 26.4 (8.2)	55 (0) 27.8 (7.5)
	12 months N (Nmissing) Mean (SD)	74 (36) 24.6 (7.4)	40 (15) 23.5 (7.4)	34 (21) 25.8 (7.2)
	21 months N (Nmissing) Mean (SD)	62 (48) 24.8 (9.5)	33 (22) 24.4 (9.7)	29 (26) 25.1 (9.3)
Self-reported falls Any past falls	**Baseline** N (Nmissing) N (%) Yes N (%) No	110 (0) 48 (43.6%) 62 (56.4%)	55 (0) 27 (49.1%) 28 (50.9%)	55 (0) 21 (38.2%) 34 (61.8%)
Number of past falls, per patient	N (Nmissing) N (%) 1N (%) 2N (%) Multiple	38 (10) 29 (76.3%) 7 (18.4%) 2 (5.2%)	19 (8) 16 (84.2%) 3 (15.8%) 0 (0%)	19 (2) 13 (68.4%) 4 (21.1%) 2 (10.6%)
	12 months			
Number of falls since the last visit, per patient	N (Nmissing) N (%) 1N (%) > 1	10 (0) 8 (80.0%) 2 (20.0%)	5 (0) 5 (100.0%) 0 (0.0%)	5 (0) 3 (60.0%) 2 (40.0%)
Patient Experience of Treatment (PETS) workload summary index score	**12 Months** N (Nmissing) Median (IQR)	73 (37) 23.8 (14.6, 31.1)	39 (16) 22.9 (14.3, 28.9)	34 (21) 26.5 (15.9, 35.5)
PETS Impact summary score	**12 Months** N (Nmissing) Median (IQR)	73 (37) 32.5 (17.5, 50.0)	39 (16) 30.0 (10.6, 45.0)	34 (21) 38.8 (20.6, 54.4)
PHQ-4 Anxiety subscale score (0 = best health to 6 = worst health)	**Baseline** N (Nmissing) Median (IQR)	105 (5) 3.0 (1.0, 4.0)	53 (2) 3.0 (1.0, 5.0)	52 (3) 2.0 (0.0, 4.0)
	12 months N (Nmissing) Median (IQR)	71 (39) 1.0 (0.0, 3.0)	39 (16) 1.0 (0.0, 3.0)	32 (23) 2.0 (0.0, 4.0)
PHQ-4 Depression subscale score (0 = best 6 = worst health)	**Baseline** N (Nmissing) Median (IQR)	105 (5) 2.0 (0.0, 4.0)	53 (2) 2.0 (0.0, 4.0)	52 (3) 2.0 (0.0, 4.0)
	12 Months N (Nmissing) Median (IQR)	70 (40) 1.5 (0.0, 3.8)	39 (16) 1.0 (0.0, 3.0)	31 (24) 2.0 (0.0, 4.0)

CONCLUSION

Progression criteria were mostly achieved as planned. A definitive, multicentre RCT of TICC-PCP is merited, to determine whether the growing number of highly qualified independent prescriber pharmacists, supported by consultant respiratory physicians, can add value to the care and outcomes of a defined cohort of patients receiving polypharmacy. Such a trial will produce rigorous evidence of the effectiveness of home visits by pharmacy professionals, while informing service change for people with symptomatic COPD and comorbidities living at home.

DATA AVAILABILITY

No datasets were generated or analysed during the current study.

MATERIALS AVAILABILITY

Data available on reasonable request, including a wider range of baseline and follow up data, through email to the corresponding author.

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AUTHOR CONTRIBUTIONS

Conception and design: R.L., D.A., N.G. (pilot RCT and sample size), FM (process evaluation), EM (Economic analysis). Interpreted the data: R.L., D.A., A.S., FM. Drafted

the work and substantially revised it: R.L., D.A., A.S., J.M., A.Mc.P., B.S., G.C., L.A., D.N., E.R., J.A., N.G., F.H., E.Mc.I., S.O.A., F.S.M.Data acquisition and analysis: R.L., D.A., J.M., A.Mc.P., B.S., G.C., L.A., D.N., J.A., N.G., F.H., E.Mc.I., S.O.A., K.W., H.S.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS

Approved by the South East Scotland Research Ethics Committee 01. REC reference: 20/SS/0093, September 2020.

CONSENT TO PUBLICATION

All participants provided written informed consent for publishing.

ADDITIONAL INFORMATION

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