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Original research

Cluster randomised controlled trial of specialist-led integrated COPD care (INTEGR COPD)

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ABSTRACT

Objective Studies in hospital settings demonstrate that there is greater guideline adherence when care is delivered by a respiratory specialist, however, this has not been explored in primary care. The aim of this study is to determine the impact integrating respiratory specialists into primary care has on the delivery of guideline adherent chronic obstructive pulmonary disease (COPD) care.

Methods 18 general practitioner (GP) practices were randomised to provide either usual or specialist-led COPD care. Patients at participating practices were included if they had an existing diagnosis of COPD. Outcomes were measured at the individual patient level. The primary outcome was guideline adherence, assessed as achieving four or more items of the COPD care bundle. Secondary outcome measures included quality of life, number of exacerbations, number of COPD-related hospitalisations and respiratory outpatient attendances.

Results 586 patients from 10 practices randomised to the intervention and 656 patients from 8 practices randomised to the control arm of the study were included. The integration of respiratory specialists into GP practices led to a statistically significant (p<0.001) improvement in the provision of guideline adherent care when compared with usual care in this cohort (92.7% vs 70.1%) (OR 4.14, 95% CI 2.14 to 8.03).

Conclusion This is the first study to demonstrate that guideline adherence is improved through the integration of respiratory specialists into GP practices to deliver annual COPD reviews. To facilitate changes in current healthcare practice and policy, the findings of this paper need to be viewed in combination with qualitative research exploring the acceptability of specialist integration.

Trial registration number NCT03482700.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Adherence to chronic obstructive pulmonary disease (COPD) guidelines is poor in primary care as confirmed by previous studies and audits. Integrated COPD care has been shown to improve health outcomes but its impact on guideline adherence in primary care is not known.

WHAT THIS STUDY ADDS

⇒ Through rigorous randomised controlled trial methodology, we have demonstrated that adherence to COPD guidelines can be improved through the integration of respiratory specialists into general practitioner (GP) practices.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings from this study can be used to support health policies that promote the integration of respiratory specialists into GP practices.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is estimated by the British Lung Foundation to be the fifth-leading cause of death in the UK.[1] Data from Public Health England indicate that the COPD mortality rate has not decreased significantly since 2001.[2 3] Within England, there are 1.1 million people registered as having COPD,[4] however, we know there are estimates of up to 2 million more people with undiagnosed COPD.[5] Overall, the prevalence of COPD is predicted to continue increasing in the UK as far as 2030.[6]

National COPD guidelines established by the National Institute for Health and Care Excellence in the UK as well as reports issued by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) focus on approaching COPD with pharmacological and non-pharmacological treatments to improve patient outcomes.[7 8] However, current literature suggests that many patients based in primary care are not receiving guideline adherent COPD management.[9–11] The provision of non-guideline adherent treatment can lead to increased healthcare costs and place patients at risk of pneumonia through inappropriate use of inhaled steroids.[12 13] A review of prepandemic literature indicates that barriers to compliance with COPD guidelines within primary care stem from a lack of familiarity with COPD guidelines and a lack of confidence with spirometry interpretation among primary care clinicians.[9 10] More recently, limited access to spirometry in primary care due to the COVID-19 pandemic is also likely to have prevented guideline-compliant diagnoses.[14 15]

Integrated COPD care is known to lead to improved patient outcomes,[16 17] however, there are no studies exploring the impact integration has on the provision of guideline adherent care.[16] The integration of COPD specialists into primary care can potentially address the root causes of poor COPD guideline compliance; COPD specialists are more likely to be familiar with current guidelines and

have confidence with interpreting spirometry due to their greater experience in comparison to generalists working in primary care. Patients with COPD who are comanaged by respiratory specialists in secondary care and general practitioners (GPs) in primary care exhibit greater concordance with COPD guidelines.[18] The aim of the INTEGR COPD study was to test whether integration of specialists into primary care had an impact on guideline adherence.

METHODS

Study design

INTEGR COPD was a pragmatic cluster randomised controlled trial. GP practices located in East Birmingham with equal access to secondary care services were approached to participate in the study. Eighteen practices agreed to participate and were stratified according to the number of patients on their COPD registers and overall patient list size, then randomised into either the intervention or usual care (control) arms of the study using SealedEnvelope.com. Stratification based on practice population demographics was not deemed necessary as the practices included in the study shared a similar patient population. A pragmatic approach was chosen for this study so as to represent the real-world impact of integrated specialist-led COPD clinics in a primary care setting. Key domains set out in the PRECIS-2 toolkit[19] were adopted to ensure study pragmatism (online supplemental file S1).

Patient involvement

The concept of integrating respiratory specialists into GP practices was discussed with a local patient and public involvement group (clinical research ambassadors group—CRAG). Patients within CRAG suggested that the study was of interest, as they valued both specialist input and care close to home. They did not feel that sharing data pertaining to routine care with the research team was a concern. Although patients from CRAG were not directly involved in the development of the study methodology, their thoughts from the initial discussion were taken into account when designing the study.

Participants

At a cluster level, GP practices were eligible to participate in the study if they belonged to the East Birmingham Health Organisation. At the individual level, patients at participating GP practices were eligible to be included in the study if they had a diagnosis of COPD recorded in their electronic patient record (EPR). Patients were excluded from the study if they were found to have been misdiagnosed with COPD during steps conducted as part of routine care.

Eligible patients at GP practices randomised to provide usual care were recruited and consented to the study at the practice (cluster) level. Information regarding the study was posted on bulletin boards at GP practices (online supplemental file S2). Patients declining to be included in the study were able to opt out, patients who were deemed to have insufficient opportunity to opt out (eg, house bound and did not attend the GP surgery during the recruitment phase) were not included. Consenting at a practice level was deemed necessary in order to reduce interference within the control practices by the research team.

Patients at GP practices randomised to the intervention arm were contacted as per usual care for their annual COPD review by GP practice staff, at which point they were given the option to attend a specialist-led annual review at the GP practice as part of the research study in lieu of seeing their usual clinician. Patients were then recruited between December 2017 and May 2019. Consent was obtained at the individual patient level.

Usual care (control)

Usual care for patients with COPD, prior to and during the study, consisted of an annual COPD review with their GP or practice nurse at their GP practice comprising a clinical and spirometry assessment as per the local guidelines,[20] recorded in the EPR using an embedded electronic COPD review template. Virtual respiratory clinics constituted a part of routine care within the East Birmingham region. Virtual clinics were offered equally to practices randomised to the intervention and control arms of the study. The virtual clinics consisted of a multidisciplinary team meeting between primary care clinicians and respiratory specialists, which included a respiratory physician and specialist nurse. The meetings were used to promote respiratory education, discuss difficult to manage respiratory patients and review primary care COPD registers to identify patients who may have been misdiagnosed. The virtual clinics were conducted on average once a week per practice for 1 hour. Direct contact with patients within the primary care setting was not within the scope of the virtual clinics, instead patients received indirect specialist-led care as their care would be discussed with specialists.

Intervention

Patients at practices randomised to the intervention arm had their annual COPD review completed by a respiratory specialist, defined as healthcare professionals based in secondary care with specialist respiratory training, this included consultant physicians, trainee respiratory physicians and respiratory physiotherapists. The annual review was completed and recorded as per the electronic template embedded in EPR software used in usual care. The intervention was, therefore, limited only to a change in the healthcare professional delivering the annual review, all other aspects remained the same as usual care, thus allowing the intervention to reflect real-world impact. Patients were enrolled in the trial for 12 months thus received two COPD reviews (baseline and 1 year) led by respiratory specialists.

Data collection

As this study was taking a pragmatic approach, there were no controlled data collection templates used, instead data recorded routinely as part of usual care using the electronic COPD template embedded in the GP practice's software was used in both the control and intervention practices. Data recorded using the EPR software or the embedded COPD template are usually coded using Read coding, these codes were used to identify relevant patient data for extraction to be used for analysis. The data extraction protocol was designed and standardised by the local National Health Service (NHS) IT department and executed by the study-specific data manager who also conducted quality control, including seeking missing critical data items such as those informing the primary outcome. Data extraction occurred at two intervals, baseline visit and follow-up visit, data recorded up to 12 months prior to each visit was extracted. In the control arm, all data were recorded by primary care clinicians, whereas within the intervention arm, data were recorded by both the specialists and primary care clinicians.

Primary outcome measure

Guideline adherence was measured as a binary outcome: patients who received four or more items of the guideline care bundle (table 1) were deemed as having guideline adherent care.

Table 1 Guideline items and rules of adherence

Item no	Guideline item	Adherence rule
1	Influenza vaccination	Record of either receiving or declining influenza vaccine within 12 months of visit will be deemed adherent. No recording will be deemed as non-adherent.
2	Pneumococcal vaccination	Record of either receiving or declining pneumococcal vaccine at any time will be deemed adherent. No recording will be deemed as non-adherent.
3	Offer of pulmonary rehabilitation	Record of either, offer, referral, declining, commencing, completing or being unsuitable for pulmonary rehabilitation in patients with a recorded MRC dyspnoea score of 3 or higher within the previous 12 months will be deemed adherent, no recording will be deemed non-adherent. Patients with MRC dyspnoea score of 2 of less are deemed adherent for this item.
4	Offer of smoking cessation	Record of either smoking cessation advice, referral, or declining advice in patients with a recorded smoking status of current smoker within the previous 12 months will be deemed adherent, no recording will be deemed non-adherent. Patients with a never-smoker or ex-smoker status will be deemed as adherent for this item.
5a	Medication 2017 guidance	Use of LABA+ICS and LAMA with an FEV_1% predicted of <50% and/or history of Asthma is adherent. Use of LABA+ICS alone if the patient has a history of asthma is adherent. Use of LABA+ICS outside of these rules is non-adherent.
5b	Medication 2019 guidance	Use of LABA+ICS and LAMA with an eosinophil count of >300 cells/µL and/or history of asthma is adherent. Use of LABA+ICS alone if the patient has a history of asthma is adherent. Use of LABA+ICS outside of these rules is non-adherent.

FEV_1, forced expiratory volume in 1 s; ICS, inhaled corticosteroid; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist; MRC, Medical Research Council.

Guideline adherence was measured at two intervals—at baseline (using patient data recorded up to 12 months prior to the baseline visit) and at follow-up 12 months postbaseline visit.

The study took place between 2017 and 2020, during which two guidelines were available, local guidance published in 2017,[20] and promoted in the region, plus GOLD documents published in 2019.[21] The guidelines varied regarding inhaled corticosteroids, therefore, guideline adherence was measured using both local 2017 and GOLD 2019 guidelines.

Secondary outcome measures

The secondary outcomes measured changes from baseline to follow-up in: (1) frequency of acute exacerbations of COPD (AECOPD), (2) number of COPD-related hospitalisations, (3) number of respiratory outpatient attendances and (4) quality of life (QOL), scored using the COPD Assessment Test (CAT).

Sample size

No prior data on bundle completion or guideline adherence with specialist input was available from a primary care setting. Therefore, the sample size was calculated using published secondary care data where COPD admission bundles (checklist of guideline-based care) were completed in 26.8% of patients when seen by a specialist, compared with 18.2% of patients when seen by a generalist.[22] Using these figures the sample size needed to detect a difference with 80% power (α=0.05) was calculated as 369 patients per study arm. As a study of this nature has not been completed previously an exact intraclass correlation coefficient (ICC) could not be used to adjust for clustering. Therefore, as per recommendations in current literature pertaining to research in primary care, an ICC of 0.01 was selected to adjust for clustering.[23] When adjusted for clustering, with an assumed ICC of 0.01 and an estimated 1500 participants across 18 clusters, the ideal sample size was 748 patients in each arm of the study.

Statistical analysis

Analysis was completed using an intention to treat (ITT) principle. Guideline adherence was compared between the two arms of the study at baseline and follow-up using logistic regression. The secondary outcomes—CAT score and frequency of exacerbations—were measured at follow-up and compared between the two arms of the study using linear regression and Poisson regression analyses, respectively. Due to an excess of zero counts within COPD-related hospitalisations and respiratory outpatient attendances these results were analysed using zero-inflated Poisson (ZIP) regression. Secondary outcomes were also compared between guideline adherent and non-adherent populations using linear regression (CAT score), Poisson regression (exacerbation frequency) and ZIP regression (COPD-related hospitalisations and outpatient attendances). All outcome analyses were adjusted for age, gender, deprivation and baseline results. Clustering was adjusted for at the practice level by applying a random-effects model to the linear, Poisson and ZIP regression analyses.

Missing data were imputed and analysed as part of a sensitivity analysis only and was not used to generate the primary results of the study. Data within the CAT score variable were deemed to be missing at random, therefore, analysis was completed using multiple imputation of 10 generated datasets. Missing data within the exacerbation frequency variable were deemed to not be missing at random and were assumed to represent '0' exacerbations, a dataset replacing missing data within that variable with '0' exacerbations was generated and analysed as part of the sensitivity analysis. Per-protocol (PP) analyses were also completed. All analyses were performed by using Stata V.16 (StataCorp) and statistical significance was set at $p<0.05$.

Results

A total of 1458 patients were screened between December 2017 and May 2019, of whom 183 were excluded at baseline and a further 33 at follow-up due to misdiagnosis. A total of 1242 patients were included in the ITT analysis, of whom, 656 patients were recruited from control practices and 586 patients were recruited from intervention practices. The study recruitment flow diagram is presented in figure 1.

Baseline characteristics

The demographic and baseline clinical, physiological and exacerbation characteristics are presented in table 2. At baseline, patients from the control and intervention practices had similar characteristics, however, there were more missing data among patients from control practices regarding CAT score, spirometry and frequency of exacerbations.

Primary outcome

There was a greater increase in guideline adherence in the intervention group versus the control group as shown in figure 2 and table 3. At the 12-month follow-up, the OR of adherence to 2017 and 2019 guidelines was 4.14 (95% CI 2.14 to 8.03) and 5.29 (95% CI 2.76 to 10.13), respectively, in favour of the intervention versus usual care (table 3), which was statistically significant ($p<0.001$). Indicating that the intervention led to a statistically significant greater provision of guideline adherent COPD care.

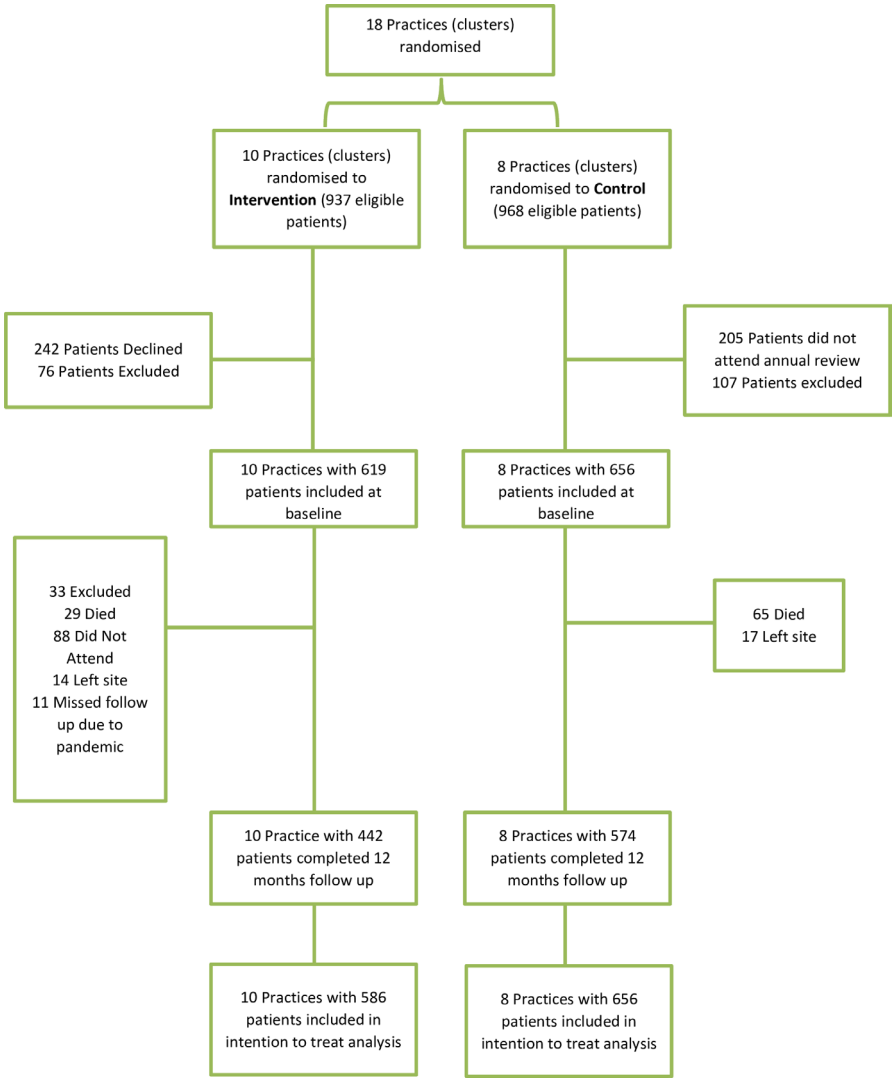

Figure 1 Study recruitment flow diagram.

Both groups showed improvement in influenza vaccination and pneumococcal vaccination from baseline to follow-up. The intervention group showed improvement in all guideline items, however, the control group worsened in attainment of guideline items regarding offer of pulmonary rehabilitation, smoking cessation and guideline adherent medication as shown in figure 3 and table 4.

Secondary outcomes

Quality of life

CAT scores were recorded less as part of usual care, thus leading to the control group having fewer scores at baseline and follow-up than the intervention group (n=250 vs 450). The CAT score at follow-up was lower in the intervention arm, the difference between intervention and control was −1.78 with a 95% CI of −2.82 to −0.73 (p=0.001) (table 5). Although statistically significant, the difference in CAT score at follow-up between intervention and control was not clinically significant. Regression analyses were repeated for this variable using 10 generated imputed datasets producing results with the same statistical and clinical significance as the ITT analysis (online supplemental file S3).

COPD-related hospitalisation

The majority of patients had no hospitalisations at baseline and follow-up in both the control and intervention group as shown in the box plot in figure 4. However, there was a statistically significant difference at follow-up with fewer hospitalisations in the control arm with an incidence rate ratio intervention to control of 1.86 (95% CI 1.38 to 2.52), p<0.001 (table 6).

COPD exacerbations

Similar to CAT, frequency of exacerbations was poorly recorded in the primary care clinical system, disproportionately affecting control practices (n=214 vs 437 exacerbation frequencies recorded at baseline and follow-up). The distribution of COPD exacerbations at baseline and follow-up for the control and intervention groups is represented in figure 4. There was no statistically significant difference in the number of exacerbations at follow-up between the control and intervention groups (table 7). Missing data were deemed to represent patients having zero exacerbations. This assumption was based on discussion with clinicians involved in entering data in the electronic records, where it emerged data was often only entered when patients had

Table 2 Demographics and baseline characteristics table for the intervention and control group

	Control (N=656)	Intervention (N=586)
Demographic characteristics		
Male n (%)	339 (52)	307 (52)
Mean age (SD)	69.7 (10.7)	67.8 (10.9)
Index of Multiple Deprivation (IMD) decile		
IMD 1st decile n (%)	350 (53)	385 (66)
IMD 2nd decile n (%)	136 (21)	95 (16)
IMD 3rd decile n (%)	76 (12)	53 (9)
IMD 4th decile n (%)	36 (6)	21 (4)
IMD 5th decile n (%)	25 (4)	16 (3)
IMD 6th decile n (%)	13 (2)	3 (1)
IMD 7th decile n (%)	9 (1)	5 (1)
IMD 8th decile n (%)	9 (1)	6 (1)
IMD 9th decile n (%)	1 (0.2)	0
IMD 10th decile n (%)	1 (0.2)	1 (0.2)
Unknown n (%)	0	1 (0.2)
Smoking status		
Smoker n (%)	281 (43)	288 (49)
Ex-smoker n (%)	337 (51)	284 (48)
Never-smoker n (%)	36 (6)	14 (2)
Not recorded n (%)	2 (0.3)	0
CAT score		
0–10 n (%)	151 (23)	159 (27)
11–20 n (%)	147 (22)	207 (35)
21–30 n (%)	67 (10)	152 (26)
31–40 n (%)	21 (3)	67 (11)
Not recorded n (%)	270 (41)	1 (0.2)
MRC Dyspnoea score		
1 n (%)	124 (19)	90 (15)
2 n (%)	223 (34)	169 (29)
3 n (%)	179 (27)	161 (27)
4 n (%)	86 (13)	135 (23)
5 n (%)	14 (2)	24 (4)
Not recorded n (%)	30 (5)	7 (1)
Spirometry		
Mean FEV_1% predicted (SD)	61.2 (19.2)	60.5 (19.6)
GOLD 1 n (%)	75 (11)	96 (16)
GOLD 2 n (%)	254 (39)	272 (46)
GOLD 3 n (%)	103 (16)	140 (24)
GOLD 4 n (%)	27 (4)	24 (4)
Not recorded n (%)	197 (30)	54 (9)
Exacerbations in 12 months prior to baseline visit		
Mean no of exacerbations (SD)	1 (1.4)	1 (1.9)
No exacerbations n (%)	186 (28)	254 (43)
1–2 exacerbations n (%)	126 (19)	200 (34)
>2 exacerbations n (%)	50 (8)	121 (21)
Exacerbation frequency not recorded n (%)	294 (45)	11 (2)
COPD-related hospitalisations in 12 months prior to baseline visit		
Mean no of hospitalisation (SD)	0.2 (0.6)	0.1 (0.5)
No hospitalisation n (%)	556 (85)	530 (90)
1–2 hospitalisations n (%)	93 (14)	51 (9)
>2 hospitalisations n (%)	7 (1)	5 (1)
Respiratory outpatient attendance in 12 months prior to baseline visit		
Mean no of respiratory outpatient attendances (SD)	0.4 (0.9)	0.2 (0.7)
No attendances n (%)	537 (82)	519 (89)
1–2 attendances	91 (14)	52 (9)
>2 attendances	28 (4)	15 (2)

Data presented as frequency (%) or mean (SD).
CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; GOLD, Global Initiative for Chronic Obstructive Lung Disease; MRC, Medical Research Council.

exacerbations and was left blank when patients had zero exacerbations. Analysis using imputed data produced results with the same clinical and statistical significance as the ITT analysis (online supplemental file S3).

Respiratory outpatient attendance

There was no statistically significant difference in attendance to respiratory outpatient clinic at follow-up between the two arms of the study (table 8). The distribution of respiratory outpatient attendances at baseline and follow-up for the control and intervention groups is represented in figure 4.

Impact of guideline adherence on secondary outcomes

Guideline adherence was associated with statistically significant but not clinically significant lower CAT score and frequency of COPD exacerbations. However, guideline adherence was also associated with statistically significant higher rate of COPD-related hospitalisations (online supplemental file S3).

Per protocol analysis

An exploratory PP analysis was completed to determine if outcomes to the intervention differed when patients completed the 12-month follow-up review as intended. The PP analysis produced similar statistical and clinical significance as the ITT analysis (online supplemental file S3).

DISCUSSION

Principal findings

We showed that integration of COPD specialists into GP practices led to a statistically significant improvement in the delivery of guideline adherent care. Prior to the intervention, guideline adherence ranged from 70% to 75%, however, 12 months following the intervention, it increased to >90%, with the change in compliance mainly being driven by alterations in pulmonary rehabilitation referral in the intervention group. Integration of COPD specialists also led to statistically lower CAT scores, although not clinically significant being less than the

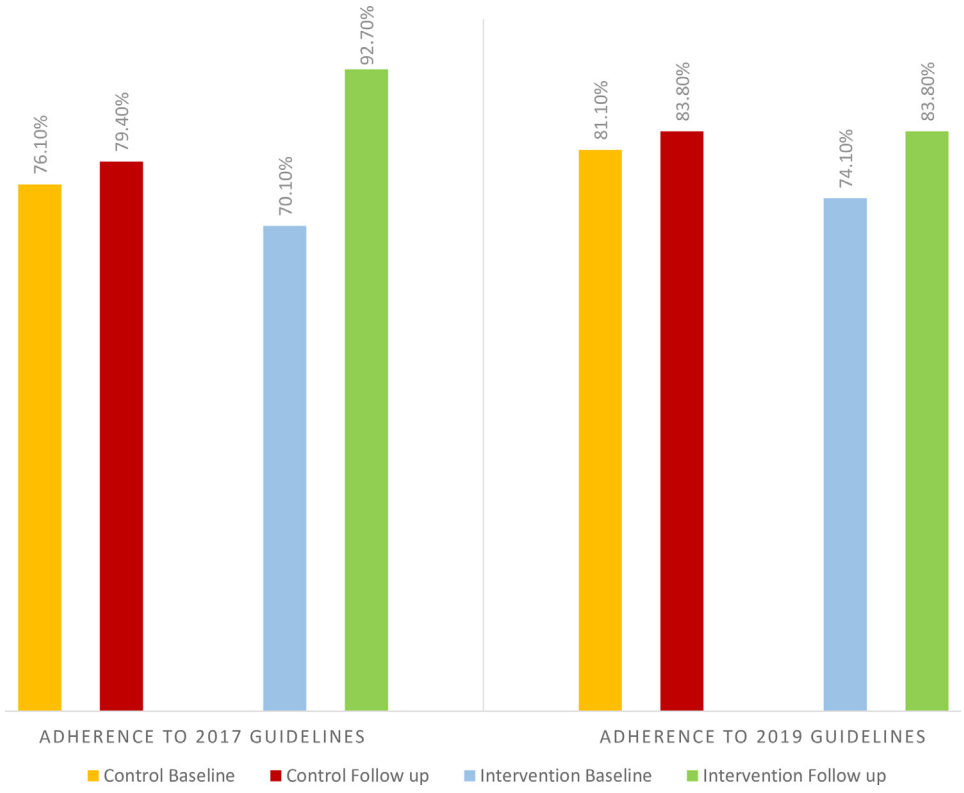

Figure 2 Comparison of adherence to 2017 and 2019 guidelines between baseline and follow-up in both the control and intervention groups. Percentage of adherent patients is shown.

minimally clinically important difference (MCID), but also led to higher rates of COPD-related hospitalisations. It is possible that adherence to guidelines was the driving factor to these secondary outcomes as we found adherence to guidelines was also associated with significantly lower CAT scores, fewer COPD exacerbations and a higher rate of COPD-related hospitalisations. However, that significance should be interpreted with caution as the change in CAT score, although statistically significant, was not clinically significant, and within the hospitalisation variable the majority of patients had no exacerbations at baseline and follow-up, therefore, change in hospitalisation frequency would have only been seen in outlier cases.

We expected guideline adherence and the intervention to be associated with lower CAT scores and fewer exacerbations, however, the higher rate of COPD-related hospitalisation was not expected. We postulated two possible factors contributing to higher rates of COPD-related hospitalisations in the intervention group. First, the integration of specialists into practices allocated to the intervention arm of the study may have diverted primary care clinicians away from COPD management, resulting in lower thresholds to refer patients to hospital for emergency admissions. Second, patient perceptions of their illness may have changed after being reviewed by a specialist in a primary care setting to the extent their threshold for attending the Accident & Emergency (A&E) department for urgent COPD care may have reduced. Both of these factors are best explored through qualitative research, which is outside of the scope of this paper.

The range of outcome metrics collected allowed us to comment on process (guideline adherence) as well as effect of process on the patient (QOL, exacerbations, admissions), which we hope will guide priorities for commissioners as well as providing informative data for patients.

Comparison to current literature

This study is the first to measure provision of guideline adherent care as a primary outcome following implementation of an integrated COPD care service in a primary care setting. The results reflect the findings from secondary care,[22] whereby completion of COPD guideline bundles and delivery of guideline adherent care was greater with specialist respiratory input.

A systematic review of integrated care for COPD has been conducted,[17] which reported a significant improvement in QOL and reduction in COPD-related hospital admissions, with no alteration of AECOPD rate, but it is difficult to directly compare our results to the included literature. The INTEGR

Table 3 Guideline adherence: comparison between and within control and intervention groups (intention to treat)

	Control (N=656)		Intervention (N=586)		Between-group OR at 12-month follow-up* (95% CI)
	Baseline n (%)	Follow-up n (%)	Baseline n (%)	Follow-up n (%)	
Adherence to 2017 guidelines	499 (76.1)	521 (79.4)	411 (70.1)	543 (92.7)	4.14 (2.14 to 8.03) **p<0.001**
Adherence to 2019 guidelines	532 (81.1)	550 (83.8)	434 (74.1)	557 (83.8)	5.29 (2.76 to 10.13) **p<0.001**

P values in bold.
*Adjusted for clustering, age, gender, deprivation and baseline guideline adherence.

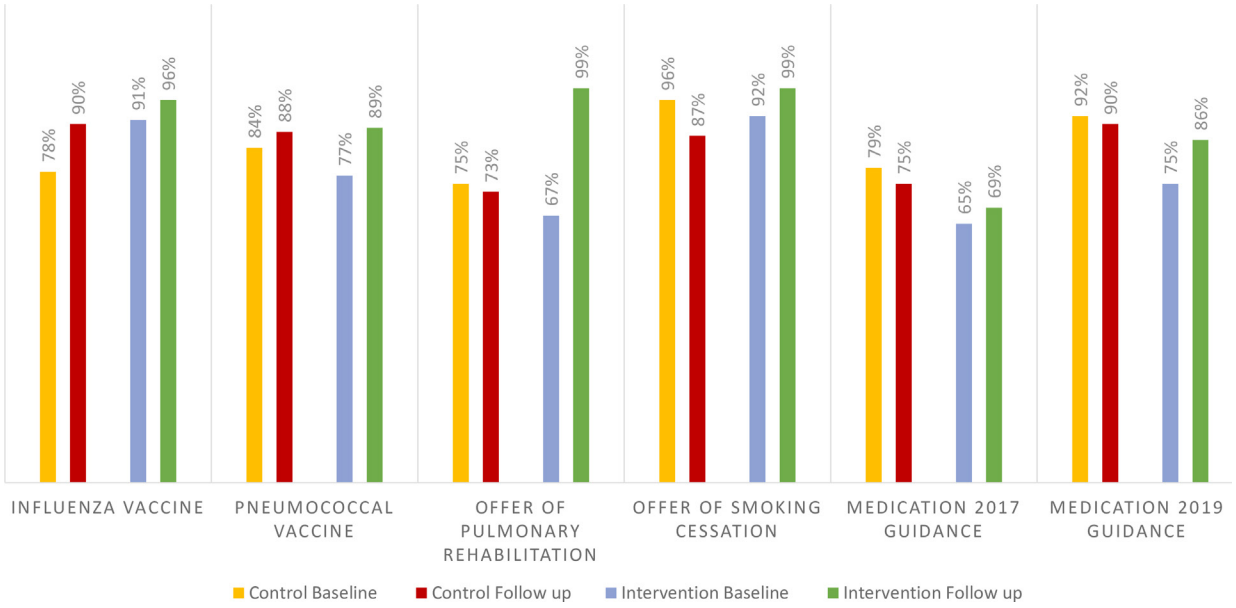

Figure 3 Comparison of adherence to each guideline item between baseline and follow-up in both the control and intervention groups. Percentage of adherent patients is shown.

COPD intervention included multiple components of integrated care, namely, diagnostic support through spirometry; education through patient self-management education and case management through clinical review and treatment optimisation. Whereas most integrated care interventions, in particular those included in the Kruis *et al*[17] systematic review, only focus on one or two components. In addition, there was access to a virtual respiratory clinic as part of usual care, which is not part of normal practice in most primary care settings, and indeed is no longer commissioned locally. Our results concurred with the Kruis *et al* systematic review regarding QOL, which was numerically, if not clinically significantly different between trial arms, and AECOPD rate, which did not differ. In addition, a recent Australian integrated COPD care study[24] with an intervention similar to INTEGR COPD also found no clinically significant change in CAT score from baseline to 12 months follow-up between integrated care and usual care. This suggests our findings with regard to QOL are likely to be robust, in the sense that QOL effects which may accrue out with effects from AECOPD are probably small, perhaps not surprising in a disease with so many influences on QOL.

Table 4 Adherence to each guideline item (intention to treat)

	Control (N=656)		Intervention (N=586)	
	Baseline n (%)	Follow-up n (%)	Baseline n (%)	Follow-up n (%)
Influenza vaccine	514 (78)	593 (90)	532 (91)	561 (96)
Pneumococcal vaccine	548 (84)	575 (88)	452 (77)	524 (89)
Offer of pulmonary rehabilitation	493 (75)	481 (73)	390 (67)	579 (99)
Offer of smoking cessation	630 (96)	573 (87)	541 (92)	583 (99)
Medication 2017 guidance	518 (79)	493 (75)	380 (65)	406 (69)
Medication 2019 guidance	601 (92)	592 (90)	439 (75)	503 (86)

Conversely, Kruis *et al* found a reduction in hospital admissions. While guideline adherent care was also associated with more COPD-related hospital admissions when compared with non-guideline adherent care it is not clear that this directly related to the intervention, since patients were not seen for the trial during AECOPD, and self-management plans issued to patients were identical between arms. The study was also not powered for this outcome. Furthermore, our integrated care offer did not include admission avoidance, unlike some studies included in the systematic review. This finding, therefore, requires more research.

It was notable that guideline adherence improved from baseline even in control practices and was at or above 80% at 12 months dependent on the guideline used, while we cannot definitively say this was due to the virtual clinics conducted in the area at the time as part of the usual care offer it is encouraging. Consistent with our interpretation that virtual clinics were helpful locally, we saw marked differences from published literature with regard to pulmonary rehabilitation where UK COPD audit found that the rate of offer of pulmonary rehabilitation was 34.5%,[25] compared with 75% at baseline in the INTEGR COPD control cohort, implying greater referral in those practices receiving the virtual service. Since a major driver of the eventual difference in guideline adherence between the two groups was pulmonary rehabilitation referral, it is possible that adoption purely of virtual clinics would eventually achieve the difference seen.

Strengths and weaknesses

The pragmatic approach taken in this study allowed it to represent real-life impact of a multicomponent integrated care intervention set in general practice. However, although multiple GP surgeries of varying size and resources were recruited, the practices were all based in one, largely deprived, region. This is a potential strength, in that we were targeting care to areas of greatest need, and many of the participating practices had never participated in research before, thus there was a potential capacity-building effect. However, the limitations were necessary to ensure usual care was similar between practices, because

Table 5 CAT score outcome: comparison between and within control and intervention groups (intention to treat)

	Control			Intervention			Between-group difference*	
CAT score outcome	Baseline mean (SD)	12-month follow-up mean (SD)	Mean change from baseline (95% CI)	Baseline mean (SD)	12-month follow-up mean (SD)	Mean change from baseline (95% CI)	Adjusted difference at follow-up (95% CI)	P value
Whole cohort	14.46 (8.51)	13.77 (7.51)	−0.35 (−1.19 to 0.48)	17.50 (9.76)	14.02 (9.71)	−3.19 (−3.90 to −2.49)	−1.78 (−2.82 to −0.73)	0.001

Control n=250; intervention n=450.
*Adjusted difference represented by using coefficient and adjusted for clustering, age, gender, deprivation and baseline cat score.
CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease.

the virtual service was not offered in exactly the same way elsewhere in the UK (there are similarities with other services now in existence), and not commissioned at all in other areas of Birmingham, where the staff funded to deliver the intervention arm were located. This reduces the ability to generalise the findings from the INTEGR COPD cohort to other areas within the UK which are less deprived or less urban in nature. The presence of virtual integrated respiratory care may also have positively impacted guideline adherence in the control arm and thus reduced differences seen between the control and intervention groups. Consequently, effects might be greater in areas with no prior or virtual integration.

Differences in the consent processes between the control and intervention practices may have led to a potential selection bias within the intervention and control cohorts. However, we felt that selection bias was unlikely to have had a significant impact on the study cohorts as the percentage of patients declining to participate in the intervention arm (26%) was similar to those who had not attended their annual COPD review in the control arm (22%). Suggesting that the majority of those who declined to participate in the study at intervention practices are likely to be patients who would normally have declined annual COPD reviews as part of usual care, therefore, the intervention and control cohorts were thought to be comparable.

A limitation in this study was that housebound patients were unable to participate as patients were required to be able to attend the GP practices for their annual COPD review in both the control and intervention practices. As a result, this study is limited to only represent ambulatory patients and cannot be generalised to the whole primary care COPD population, and this limitation should be considered when reading our conclusions.

Missing CAT scores and COPD exacerbation data were key limitations. Recording of clinical data in primary care is often coded to allow for clinical audit to ensure government targets known as quality outcomes framework (QOF) are met. QOF applies a monetary incentive for meeting targets, which are measured through the audit of clinical notes. Unlike CAT and AECOPD rate, recording of smoking status, smoking cessation advice, influenza vaccination, MRC score, spirometry and pulmonary rehabilitation were all part of QOF,[26] and as such these variables had minimal missing data. Differences in degree of missing CAT score data between control and intervention arms mean that the results pertaining to improvement in QOL should be interpreted with caution.

Due to the nature of this study, clinicians could not be blinded and were aware of their allocation to either the control or intervention arm of the trial. Clinicians working within practices allocated to the control arm had the potential of being influenced

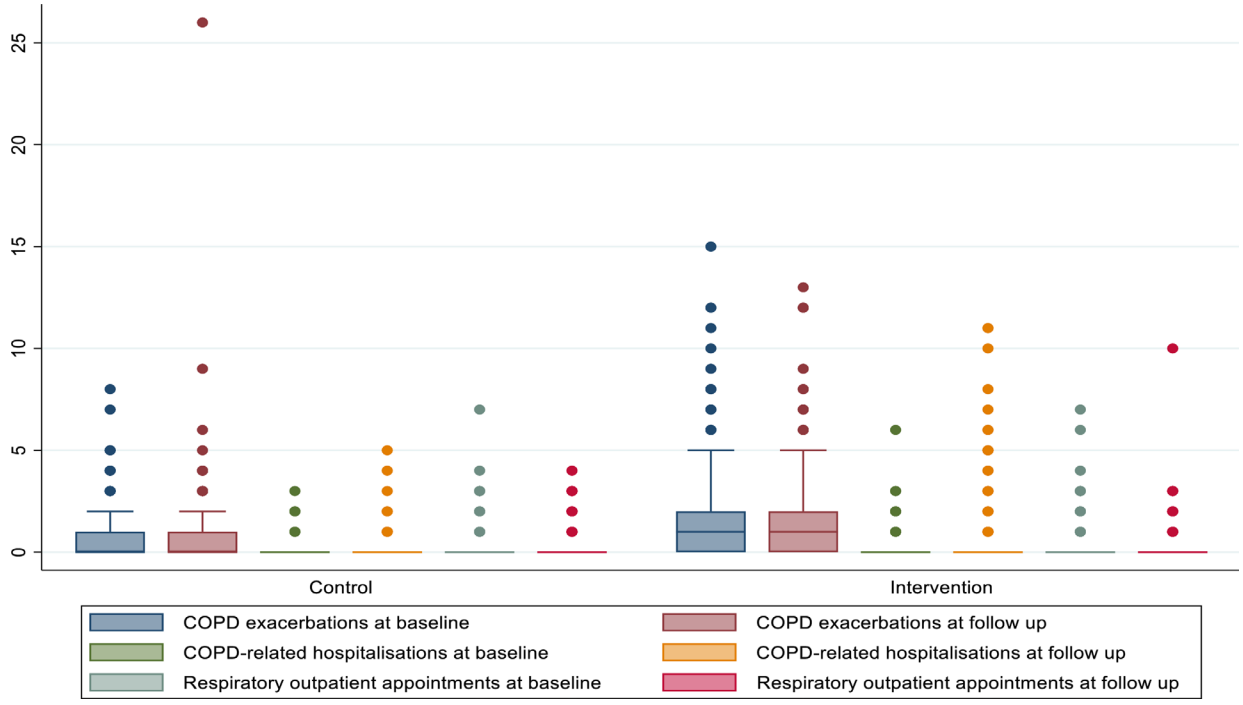

Figure 4 Boxplot presenting number of COPD exacerbations, COPD-related hospitalisations and respiratory outpatient appointments at baseline and follow-up for control and intervention groups. COPD, chronic obstructive pulmonary disease.

Table 6 COPD-related hospitalisations outcome: comparison between control and intervention groups (intention to treat)

	Between-group difference*	
COPD-related hospitalisations outcome	Adjusted difference at follow-up (95% CI)	P value
Whole cohort	1.86 (1.38 to 2.52)	<0.001

Control n=656; intervention n=586.
*Calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline COPD-related hospitalisations.
COPD, chronic obstructive pulmonary disease.

Table 8 Respiratory outpatient attendance outcome: comparison between control and intervention groups (intention to treat)

	Between-group difference*	
Respiratory outpatient attendance outcome	Adjusted difference at follow-up (95% CI)	P value
Whole cohort	0.93 (0.65 to 1.32)	0.67

Control n=656; intervention n=586.
*Calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline respiratory outpatient attendances.

to change their clinical practice due to their awareness of the study and knowledge of their medical records being scrutinised as part of the trial, thus not representing true real-life practice. However, baseline data were collected through extraction of medical records up to 12 months prior to the practice's involvement in the trial, therefore, would not have been influenced by the trial. As there was minimal change in the primary and secondary outcome variables between baseline and follow-up in the control arm, we can assume that the impact of unblinding clinicians in the control arm was minimal. Specialists delivering the intervention operated at multiple practices allocated to the intervention arm the study. As a result, the ratio of patients to clinician was higher in the intervention arm compared with the control arm. Due to this higher ratio, a clinician's bias had the potential to influence more patients and the clinical details recorded. To mitigate against this potential bias, patients were seen by different members of the specialist team at baseline and follow-up, in order to minimise the potential influence of a single clinician's bias.

Extraction of data from medical records was completed by the trial data manager, however, the data extraction process was designed and standardised by information technology (IT) teams employed by the NHS trust and clinical commissioning group (CCG). The extraction process was applied to both control and intervention practices and due to its standardised nature, it was not open to being influenced by the trial data manager, thus strengthening the integrity of the data obtained.

Implications on practice and future research

Although this study is posed as a comparison between integrated care and usual care, a more appropriate description would be a comparison between 'real' integration and 'virtual' integration. Virtual integration provided patients with indirect specialist-led care, however, with the addition of direct specialist-led care or 'real' integrated care the intervention significantly improved the provision of guideline adherent care. Within this cohort, guideline adherence was shown to have an impact on QOL, COPD exacerbations and COPD-related hospitalisations. However, the difference in QOL outcome between virtual and real integration was not clinically significant and virtual integration had fewer hospitalisations at follow-up. Therefore, at least theoretically, a hybrid model involving components of both virtual and real integration should be tested against a comparator with no integrated care to determine the true effectiveness of integrated care. The impact of integrating specialists into general practice is described in this study through changes in numerical data, however, it does not represent the human impact. This aspect of the study does not represent whether the intervention changed clinician behaviours and perceptions, nor did it represent acceptability of the intervention among patients and staff in GP practices. These factors are important to determine whether integrating respiratory specialists into primary care would be successful or not which we have addressed through parallel qualitative research. Using a combination of both qualitative and quantitative results would provide better guidance for future integrated care interventions, but it was beyond the scope of a single paper to report all data together.

Table 7 COPD exacerbations outcome: comparison between control and intervention groups (intention to treat)

	Between-group difference*	
COPD exacerbations outcome	Adjusted difference at follow-up (95% CI)	P value
Whole cohort	1.14 (0.87 to 1.49)	0.34

Control n=214; intervention n=437.
*Calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline number of exacerbations.
COPD, chronic obstructive pulmonary disease.

CONCLUSION

Within this cohort, integrating a respiratory specialist into general practices significantly improved the provision of guideline adherent care. The provision of guideline adherent care led to an impact on QOL, COPD exacerbations and COPD-related hospitalisations, however, further studies with larger cohorts are needed to determine if this impact is clinically significant.

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Contributors AMT: procured study funding. KP, AMT, AP and APD: prepared the manuscript. KP, RGE, HB, PRE, AMT and AP: trial recruitment. KP and AS: statistical analysis. KP and AMT act as guarantors of the work. All authors have read and approved the manuscript.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was the study was approved by West Midlands South Birmingham Research Ethics Committee (REC 17/WM/0342). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Anonymised study data will be made available on reasonable request to the corresponding author.

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Supplement 1 - PRECIS-2 Domains scores and rationale

PRECIS-2 Domain	Score	Rationale
Eligibility Criteria- to what extent are the participants in the trial similar to those who would receive this intervention if it was part of usual care?	5	Patients were eligible for the study if they had a diagnosis of COPD and attended routine annual COPD review with their GP or practice nurse. If the intervention was implemented as usual care the same cohort of patients would receive the intervention.
Recruitment Path- how much extra effort is made to recruit participants over and above what that would be used in the usual care setting to engage with patients?	5	Minimal additional effort was required to recruit patients for the study. Patients were recruited for the study through the usual appointment booking system used in usual care, whereby those due for their annual review were contacted by the practice receptionist and were offered to be seen by a specialist as part of a trial.
Setting- how different is the setting of the trial and the usual care setting?	5	There was no difference between the trial setting and usual care. The intervention was being delivered within GP practices and using practice resources, which would have been used as part of usual care.
Organisation- how different are the resources, provider expertise and the organisation of care delivery in the intervention arm of the trial and those available in usual care?	4	There was no difference between the resources used or available in the intervention arm and usual care arm of the study. The delivery of the intervention required respiratory specialists with expertise in respiratory medicine, which is not part of usual care. However, the mode of care delivery was identical between the intervention and usual care as both used standardized COPD templates to guide the review, which is part of usual care.
Flexibility (Delivery)- how different is the flexibility in how the intervention is delivered and the flexibility likely in usual care?	5	As the intervention was being delivered within the same setting as usual care and was bound by the same timing and room availability constraints there was no difference in flexibility of care delivery between intervention and usual care.
Flexibility (Adherence)- how different is the flexibility in how participants must adhere to the intervention and the flexibility likely in usual care?	5	Measures to ensure adherence to the intervention were identical to usual care. The measures used were messages and calls from GP receptionists to patients reminding them to book and attend for their annual COPD review, which was usual practice.
Follow up- how different is the intensity of measurement and follow-up of participants in the trial and the likely follow-up in usual care?	5	There was no difference in follow up intensity between intervention and usual care. Patients were offered annual follow up as per usual care and measurements carried out in the intervention were as per local COPD guidelines used in usual care.
Primary outcome- to what extent is the trial's primary outcome relevant to participants?	5	The primary outcome is guideline adherence. The outcome can be measured in a usual care setting without additional expertise or resources as it is based on data collected as part of usual care. It is very relevant to participants as it reflects the quality of evidence-based care they have received.
Primary analysis- to what extent are all data included in the analysis of the primary outcome?	5	Primary outcome data will be analysed using an intention to treat approach, using all available data of patients who were deemed eligible and consented to participate in the trial.

Heartlands Hospital NHS
Part of University Hospitals Birmingham NHS Foundation Trust

Do you have Chronic Obstructive Pulmonary Disease (COPD)?

Do you want to shape the future of COPD care?

Overview

Birmingham Heartlands Hospital part of University Hospitals NHS Foundation Trust is excited to be partnering with local healthcare providers to evaluate the quality of care patients with COPD receive in different healthcare settings.

What do we hope to achieve with this project?

We have set ourselves a number of goals, which include:

- Comparing respiratory specialist care in the primary care setting with 'usual' care for patients with COPD, to determine if patients with COPD are receiving care which follows current guidelines.
- Evaluating if guideline based care leads to better health outcomes for patients with COPD.
- Determining if respiratory specialist care leads to improved quality of life for patients with COPD.

Who is involved?

The project is a partnership between:

- Birmingham Heartlands Hospital who will provide leadership to the project, as well as clinical input, academic oversight and technical support.
- Local participating GPs, who will play a key role in recruiting patient and will contribute with clinical input and leadership.

What is our starting point?

This study will look at the quality of care patients with COPD receive in the primary care setting. In particular, this study will compare respiratory specialist care to 'usual care'. This data will be used to answer a number of research questions, which in turn will allow us to identify changes that should bring benefits to those living with COPD. We will publish our findings in research journals and share these at academic conferences, so that a broader audience can learn from our research. These findings will also be available on the hospital website.

How will the data be collected?

General practices already routinely collect treatment data which we have identified as being vital to evaluating the quality of care patients with COPD receive. For the purposes of this study, this information will be extracted by NHS IT staff in each participating NHS organisation. Before the data is securely transmitted to a special research database, the IT staff will carry out a number of processes to ensure it is not identifiable to anyone outside their organisation. This process (which is called 'pseudonymisation') replaces identifiable information (such as name, address and date of birth) with versions that do not allow the individual to be identified. The data will also be encrypted on our secure server where access will be restricted to designated individuals.

What type of data will you collect?

This project will focus on patients with COPD. The information we collect will focus on the care patients with COPD receive including tests and treatments (e.g. clinic appointments, laboratory tests, scans, prescriptions), and their outcomes (e.g. lung function, progression after treatment, complications etc.). To help us better understand how patients with COPD progress we will collect data regarding the number of unscheduled healthcare consultations, defined as emergency primary care appointments, emergency department attendance at hospital and hospital admissions. This data will give us a better idea of how patients with COPD progress when receiving respiratory specialist care compared to 'usual care'.

How do I know my data is safe?

All data that could identify you will be removed while the data is still held within the NHS, and will be thoroughly checked before leaving the NHS database. Once this has been done, it will be securely transmitted and stored within a system that is both physically secure from intruders and protected by firewalls to prevent access from outsiders. Access to the data will be restricted to a list of specially trained individuals approved by the NHS. These security provisions have been approved by the hospital Information Governance Committee. This study has been reviewed and received favourable opinion by West Midlands – South Birmingham Research Ethics Committee

How do I know my data won't be misused?

Your data will only be used to answer specific research and service redesign questions that have been defined and approved by all members of the project's Governance Board. This Governance Board consists of members from all partner organisations, with additional patient and public health representatives. We have taken a number of measures to ensure compliance with national policy and legislation on patient privacy and data protection. At all times, your rights under the Data Protection Act will be upheld.

How will this benefit me?

The project will provide vital information regarding the quality of care patients with COPD receive in the primary care setting and will provide a comparison between respiratory specialist care and 'usual care'. This will allow us to evaluate if guideline based care leads to better health outcomes and quality of life in patients with COPD. We can then use this knowledge to improve clinical outcomes for patients with COPD and improve the coordination of care across services.

What if I do not want to participate?

If you would rather not participate in the project, please inform your GP to ensure that your data will be excluded from all future analysis. You can choose to opt out at any time. If you opt-out, your information will remain confidential and will not be used in any further future data analysis undertaken as part of this project. In order to ensure your data is successfully excluded, and not accidentally re-incorporated at a future date, we will maintain a list of the codenames for patients that have opted out – these codenames will be unidentifiable outside of the NHS.

Supplement 3 – Supplementary data tables

Impact of guideline adherence on secondary outcomes

Impact of adherence/non-adherence at baseline	2017 Guidelines			2019 Guideline		
	Coeff (95%CI)	IRR (95%CI)	*p*-Value	Coeff (95%CI)	IRR (95%CI)	*p*-Value
CAT Score	-1.98 (-3.34 – -0.61)	N/A	0.005	-1.41 (-2.89 – 0.06)	N/A	0.05
COPD-related Hospitalisations*	N/A	1.22 (1.04 – 1.44)	0.014	N/A	1.22 (1.04 – 1.44)	0.016
COPD exacerbations	N/A	0.75 (0.65 – 0.86)	<0.001	N/A	0.80 (0.70 – 0.92)	0.002
Respiratory outpatient attendances*	N/A	0.86 (0.71 – 1.04)	0.13	N/A	0.99 (0.84 – 1.17)	0.95

Table 1 Impact of adherence to 2017 and 2019 guidelines: comparison of secondary outcomes between guideline adherent and non-adherent patients at baseline (intention-to-treat). Coeff: Coefficient; CI: Confidence Interval; IRR: Incidence rate ratio. All outcomes have been adjusted for clustering, age, gender, deprivation, and randomisation group. *adjusted for excess zero count. Coefficients and IRRs are of guideline adherence to non-adherence.

Per protocol data analysis outputs

	Baseline		12 month Follow up		Between group odds ratio at 12 month follow up* (95%CI)
	Control n(%)	Intervention n(%)	Control n(%)	Intervention n(%)	
Adherence to 2017 Guidelines	441 (76.8)	323 (72.9)	456 (79.4)	423 (95.5)	6.19 (2.88-13.29) **p=<0.0001**
Adherence to 2019 Guidelines	467 (81.3)	345 (77.8)	480 (83.6)	434 (97.9)	10.97 (4.32-27.89) **p=<0.0001**

Table 2 Guideline adherence at baseline and follow up (per protocol). Control N=574; Intervention N=443; CI: Confidence interval. *-adjusted for clustering, age, gender, deprivation and baseline guideline adherence.

	Control (N=574)		**Intervention (N=443)**	
	Baseline n(%)	**Follow up n(%)**	**Baseline n(%)**	**Follow up n(%)**
Influenza vaccine	451 (79)	526 (92)	407 (92)	435 (98)
Pneumococcal vaccine	479 (83)	506 (88)	345 (78)	416 (94)
Offer of pulmonary rehabilitation	441 (77)	421 (73)	310 (70)	438 (99)
Offer of smoking cessation	554 (97)	497 (87)	410 (93)	442 (99)
Medication 2017 guidance	454 (79)	428 (75)	288 (65)	299 (67)
Medication 2019 guidance	526 (92)	517 (90)	347 (78)	389 (88)

Table 3 Adherence to each guideline item at baseline and follow up (per protocol).

CAT score outcome	Control				Intervention				Between-group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	244	14.15 (8.29)	13.82 (7.53)	-0.33 (-1.18 – 0.52)	442	17.27 (9.66)	14.02 (9.68)	-3.24 (-3.96 – -2.52)	-1.82 (-2.89 – -0.76)	0.001

Table 4 CAT score outcome: comparison between and within control and intervention groups (per-protocol). SD: Standard deviation; CI: Confidence interval; *calculated using coefficient and adjusted for clustering, age, gender, deprivation, and baseline CAT score.

COPD-related hospitalisations outcome – Adjusted for zero counts	Control				Intervention				Between group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	74	0.77 (1.33)	1.31 (0.62)	-0.54 (-0.86 – -0.22)	38	1.39 (0.95)	1.11 (2.44)	-0.28 (-1.03 – 0.46)	2.43 (1.67 – 3.54)	<0.001

Table 5 COPD-related hospitalisations outcome adjusted for excess zero count: comparison between and within control and intervention groups (per-protocol). SD: Standard deviation; CI: Confidence interval; *calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline COPD related hospitalisations.

COPD Exacerbations outcome	Control				Intervention				Between group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	209	0.89 (1.34)	1.00 (2.18)	0.11 (-0.19 – 0.42)	428	1.44 (2.03)	1.40 (1.96)	-0.04 (-0.22 – 0.14)	1.12 (0.86 – 1.46)	0.38

Table 6 COPD exacerbations outcome: comparison between and within control and intervention groups (per-protocol). SD: Standard deviation; CI: Confidence interval; *calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline number of exacerbations.

Respiratory outpatient attendance outcome	Control				Intervention				Between group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	574	0.32 (0.87)	0.28 (0.73)	-0.04 (-0.11 – 0.01)	443	0.20 (0.71)	0.18 (0.71)	-0.02 (-0.11 – 0.07)	0.71 (0.42 – 1.18)	0.19

Table 7 Respiratory outpatient attendance outcome: comparison between and within control and intervention groups (per-protocol). SD: Standard deviation; CI: Confidence interval; *calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline respiratory outpatient attendances.

Respiratory outpatient attendance outcome – Adjusted for zero count	Control				Intervention				Between group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	99	1.88 (1.22)	1.18 (1.160	-0.70 (-0.96 – -0.43)	49	1.84 (1.26)	0.51 (0.92)	-1.33 (-1.77 – -0.89)	0.76 (0.49 – 1.19)	0.23

Table 8 Respiratory outpatient attendance outcome adjusted for excess zero counts: comparison between and within control and intervention groups (per-protocol). SD: Standard deviation; CI: Confidence interval; *calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline respiratory outpatient attendances.

Impact of adherence/non-adherence at baseline	2017 Guidelines			2019 Guideline		
	Coeff (95%CI)	IRR (95%CI)	*p*-Value	Coeff (95%CI)	IRR (95%CI)	*p*-Value
CAT Score	-2.43 (-3.95 - -0.91)	N/A	0.002	-1.64 (-3.31 – 0.03)	N/A	0.05
COPD-related Hospitalisations*	0.13 (-0.06 – 0.32)	1.14 (0.94 – 1.38)	0.19	0.09 (-0.10 – 0.28)	1.09 (0.90 – 1.32)	0.36
COPD exacerbations	-0.33 (-0.48 – -0.17)	0.72 (0.62 – 0.84)	<0.001	-0.22 (-0.38 – -0.05)	0.80 (0.69 – 0.95)	0.01
Respiratory outpatient attendances*	-0.01 (-0.28 – 0.26)	0.99 (0.75 – 1.29)	0.92	-0.01 (-0.31 – 0.29)	0.99 (0.73 – 1.34)	0.94

Table 9 Impact of adherence to 2017 and 2019 guidelines: comparison of secondary outcomes between guideline adherent and non-adherent patients at baseline (per-protocol). Coeff: Coefficient; CI: Confidence Interval; IRR: Incidence rate ratio. All outcomes have been adjusted for clustering, age, gender, deprivation, and randomisation group. *adjusted for excess zero count. Coefficients and IRRs are of guideline adherence to non-adherence.

Analysis of CAT score variable with multiply imputed datasets

CAT score outcome	Control			Intervention			Between-group difference*	
	Number of patients	Baseline Mean (95%CI)	12 Month Follow up Mean (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	656	14.40 (13.64 – 15.16)	14.28 (13.45 – 15.10)	586	17.49 (16.70 – 18.28)	14.40 (13.59 – 15.22)	-2.12 (-3.68 - -0.56)	0.008

Table 10 CAT score outcome: comparison between and within control and intervention groups using multiply imputed datasets (intention-to-treat). SD: Standard deviation; CI: Confidence interval; *Adjusted difference represented by using coefficient and adjusted for clustering, age, gender, deprivation and baseline CAT score.

Impact of adherence/non-adherence on CAT score	2017 Guideline		2019 Guideline	
	Coeff (95%CI)	*p*-Value	Coeff (95%CI)	*p*-Value
At Baseline	-2.02 (-3.42 - -0.62)	0.005	-1.30 (-2.85 – 0.25)	0.10

Table 11 Impact of adherence to 2017 and 2019 guidelines on CAT score using multiply imputed datasets (intention-to-treat). Coeff: Coefficient; CI: Confidence Interval. All outcomes have been adjusted for clustering, age, gender, deprivation, and randomisation group. Coefficients are of guideline adherence to non-adherence.

Analysis of COPD Exacerbations with imputed data

COPD Exacerbations outcome – Adjusted for excess zeros	Control				Intervention				Between group difference*	
	Number of patients	Baseline Mean (SD)	12 Month Follow up Mean (SD)	Mean change from baseline (95%CI)	Number of patients	Baseline Mean (SD)	12 month follow up Mean (SD)	Mean change from baseline (95%CI)	Adjusted difference at follow up (95%CI)	*p*-Value
Whole cohort	656	0.56 (1.16)	0.46 (1.48)	0.09 (-0.04 – 0.23)	586	1.38 (1.91)	1.06 (1.82)	0.32 (0.17 – 0.48)	1.10 (0.90 – 1.35)	0.34

Table 12 COPD exacerbations outcome: comparison between and within control and intervention groups using imputed data (intention-to-treat). SD: Standard deviation; CI: Confidence interval; *calculated using incidence rate ratio and adjusted for clustering, age, gender, deprivation and baseline number of exacerbations.