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Case-finding and improving patient outcomes for chronic obstructive pulmonary disease in primary care: the BLISS research programme including cluster RCT

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Abstract

Case-finding and improving patient outcomes for chronic obstructive pulmonary disease in primary care: the BLISS research programme including cluster RCT

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Background: Chronic obstructive pulmonary disease is a major contributor to morbidity, mortality and health service costs but is vastly underdiagnosed. Evidence on screening and how best to approach this is not clear. There are also uncertainties around the natural history (prognosis) of chronic obstructive pulmonary disease and how it impacts on work performance.

Objectives: Work package 1: to evaluate alternative methods of screening for undiagnosed chronic obstructive pulmonary disease in primary care, with clinical effectiveness and cost-effectiveness analyses and an economic model of a routine screening programme. Work package 2: to recruit a primary care chronic obstructive pulmonary disease cohort, develop a prognostic model [Birmingham Lung Improvement StudieS (BLISS)] to predict risk of respiratory hospital admissions, validate an existing model to predict mortality risk, address some uncertainties about natural history and explore the potential for a home exercise intervention. Work package 3: to identify which factors are associated with employment, absenteeism, presenteeism (working while unwell) and evaluate the feasibility of offering formal occupational health assessment to improve work performance.

Design: Work package 1: a cluster randomised controlled trial with household-level randomised comparison of two alternative case-finding approaches in the intervention arm. Work package 2: cohort study – focus groups. Work package 3: subcohort – feasibility study.

Setting: Primary care settings in West Midlands, UK.

Participants: Work package 1: 74,818 people who have smoked aged 40–79 years without a previous chronic obstructive pulmonary disease diagnosis from 54 general practices. Work package 2: 741 patients with previously diagnosed chronic obstructive pulmonary disease from 71 practices and

participants from the work package 1 randomised controlled trial. Twenty-six patients took part in focus groups. Work package 3: occupational subcohort with 248 patients in paid employment at baseline. Thirty-five patients took part in an occupational health intervention feasibility study.

Interventions: Work package 1: targeted case-finding – symptom screening questionnaire, administered opportunistically or additionally by post, followed by diagnostic post-bronchodilator spirometry. The comparator was routine care. Work package 2: twenty-three candidate variables selected from literature and expert reviews. Work package 3: sociodemographic, clinical and occupational characteristics; occupational health assessment and recommendations.

Main outcome measures: Work package 1: yield (screen-detected chronic obstructive pulmonary disease) and cost-effectiveness of case-finding; effectiveness of screening on respiratory hospitalisation and mortality after approximately 4 years. Work package 2: respiratory hospitalisation within 2 years, and barriers to and facilitators of physical activity. Work package 3: work performance – feasibility and acceptability of the occupational health intervention and study processes.

Results: Work package 1: targeted case-finding resulted in greater yield of previously undiagnosed chronic obstructive pulmonary disease than routine care at 1 year [$n = 1278$ (4%) vs. $n = 337$ (1%), respectively; adjusted odds ratio 7.45, 95% confidence interval 4.80 to 11.55], and a model-based estimate of a regular screening programme suggested an incremental cost-effectiveness ratio of £16,596 per additional quality-adjusted life-year gained. However, long-term follow-up of the trial showed that at ≈ 4 years there was no clear evidence that case-finding, compared with routine practice, was effective in reducing respiratory admissions (adjusted hazard ratio 1.04, 95% confidence interval 0.73 to 1.47) or mortality (hazard ratio 1.15, 95% confidence interval 0.82 to 1.61). Work package 2: 2305 patients, comprising 1564 with previously diagnosed chronic obstructive pulmonary disease and 741 work package 1 participants (330 with and 411 without obstruction), were recruited. The BLISS prognostic model among cohort participants with confirmed airflow obstruction ($n = 1894$) included 6 of 23 candidate variables (i.e. age, Chronic Obstructive Pulmonary Disease Assessment Test score, 12-month respiratory admissions, body mass index, diabetes and forced expiratory volume in 1 second percentage predicted). After internal validation and adjustment (uniform shrinkage factor 0.87, 95% confidence interval 0.72 to 1.02), the model discriminated well in predicting 2-year respiratory hospital admissions (c -statistic 0.75, 95% confidence interval 0.72 to 0.79). In focus groups, physical activity engagement was related to self-efficacy and symptom severity. Work package 3: in the occupational subcohort, increasing dyspnoea and exposure to inhaled irritants were associated with lower work productivity at baseline. Longitudinally, increasing exacerbations and worsening symptoms, but not a decline in airflow obstruction, were associated with absenteeism and presenteeism. The acceptability of the occupational health intervention was low, leading to low uptake and low implementation of recommendations and making a full trial unfeasible.

Limitations: Work package 1: even with the most intensive approach, only 38% of patients responded to the case-finding invitation. Management of case-found patients with chronic obstructive pulmonary disease in primary care was generally poor, limiting interpretation of the long-term effectiveness of case-finding on clinical outcomes. Work package 2: the components of the BLISS model may not always be routinely available and calculation of the score requires a computerised system. Work package 3: relatively few cohort participants were in paid employment at baseline, limiting the interpretation of predictors of lower work productivity.

Conclusions: This programme has addressed some of the major uncertainties around screening for undiagnosed chronic obstructive pulmonary disease and has resulted in the development of a novel, accurate model for predicting respiratory hospitalisation in people with chronic obstructive pulmonary disease and the inception of a primary care chronic obstructive pulmonary disease cohort for longer-term follow-up. We have also identified factors that may affect work productivity in people with chronic obstructive pulmonary disease as potential targets for future intervention.

Future work: We plan to obtain data for longer-term follow-up of trial participants at 10 years. The BLISS model needs to be externally validated. Our primary care chronic obstructive pulmonary disease cohort is a unique resource for addressing further questions to better understand the prognosis of chronic obstructive pulmonary disease.

Trial registration: Current Controlled Trials ISRCTN14930255.

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Contents

List of tables	xv
List of figures	xvii
List of abbreviations	xix
Plain English summary	xxi
Scientific summary	xxiii
SYNOPSIS	1
Background	1
Overview of research programme	1
<i>Work package 1: clinical trial to evaluate case-finding; TargetCOPD trial</i>	1
<i>Work package 2: Birmingham primary care chronic obstructive pulmonary disease cohort</i>	3
<i>Work package 3: chronic obstructive pulmonary disease and occupational performance</i>	3
Work package 1: clinical trial to evaluate case-finding – TargetCOPD trial	5
Objective (i): to ascertain the clinical effectiveness and cost-effectiveness of targeted case-finding (opportunistic or active) compared with routine primary care (work package 1i, published trial report)	5
<i>Rationale</i>	5
<i>What we did</i>	5
<i>What we found</i>	6
<i>Strengths and limitations</i>	6
Objective (ii): to develop a model (using Markov decision analysis) to compare the cost-effectiveness of a systematic case-finding programme with current practice (work package 1ii, published)	6
<i>Rationale</i>	6
<i>What we did</i>	6
<i>What we found</i>	7
<i>Strengths and limitations</i>	7
Objective (iii): to explore the views of (a) patients invited to take part in case-finding, in terms of the process and outcomes (work package 1iii, published), and (b) primary care staff, in relation to case-finding (work package 1iii, published)	7
<i>Rationale</i>	7
<i>What we did</i>	7
<i>What we found</i>	8
<i>Strengths and limitations</i>	8
Objective (iv): to describe the clinical management of screen-detected chronic obstructive pulmonary disease patients in primary care and compare management in those who were versus those who were not on the practice chronic obstructive pulmonary disease registers (work package 1iv, manuscript submitted)	8
<i>Rationale</i>	8
<i>What we did</i>	9
<i>What we found</i>	9
<i>Strengths and limitations</i>	11

Objective (v): to assess the long-term effectiveness of case-finding for chronic obstructive pulmonary disease on respiratory hospitalisations and mortality (work package 1v, manuscript in preparation) and objective (vi): to compare outcomes (including health-related quality of life) among screen-detected chronic obstructive pulmonary disease patients in primary care who were managed adequately by their general practitioner (based on the practice chronic obstructive pulmonary disease registers) with those who were not	12
<i>Rationale</i>	12
<i>What we did</i>	12
<i>What we found</i>	13
<i>Strengths and limitations</i>	13
Additional outputs and published analyses related to work package 1	13
<i>Jordan et al.</i>	14
<i>Miller et al.</i>	14
<i>Haroon et al.</i>	14
<i>Haroon et al.</i>	14
<i>Haroon et al.</i>	14
<i>Haroon et al.</i>	14
Work package 2: the Birmingham primary care chronic obstructive pulmonary disease cohort	15
Objective (i): to recruit a cohort of 2000 new and existing chronic obstructive pulmonary disease patients from general practices in the West Midlands (work package 2, linked to work package 1, published)	15
<i>Rationale</i>	15
<i>What we did</i>	15
<i>What we found</i>	18
<i>Strengths and limitations</i>	18
Objective (ii): to test the validity of existing chronic obstructive pulmonary disease prognostic models in a primary care chronic obstructive pulmonary disease population (work package 2, published); and objective (iii): to develop a prognostic model (BLISS index) to predict respiratory hospitalisations suitable for a primary care population (work package 2, drafted, see <i>Appendix 4</i>)	18
<i>Rationale</i>	18
<i>What we did (objective ii)</i>	19
<i>What we found (objective ii)</i>	19
<i>What we did (objective iii)</i>	19
<i>What we found (objective iii)</i>	20
<i>Strengths and limitations</i>	20
Objective (iv): to explore barriers to and enablers of participation in physical activity among people with chronic obstructive pulmonary disease in primary care (work package 2, published)	20
<i>Rationale</i>	20
<i>What we did</i>	21
<i>What we found</i>	21
<i>Strengths and limitations</i>	21
Other collaborations and analyses of cohort data	21
<i>Cohort data used for analyses leading to a PhD thesis: Buni</i>	21
<i>Collaboration with Professor Mike Thomas from the University of Southampton: Brien et al.</i>	23
<i>Linked trial funded through the NIHR National School of Primary Care Research: Jolly et al.</i>	23
<i>Dickens et al.</i>	23
<i>Cohort data used by Master of Public Health students: Khan et al.</i>	23
<i>Cohort data used as part of a PhD thesis: Kosteli</i>	23

Work package 3: chronic obstructive pulmonary disease and occupational performance	25
Objective (i): to examine factors associated with employment (published), absenteeism and presenteeism (published) among COPD patients of working age (work package 3)	25
<i>Rationale</i>	25
<i>What we did</i>	25
<i>What we found</i>	25
<i>Strengths and limitations</i>	26
Objective (ii): to examine how disease progression (lung function decline, exacerbation) over time is associated with occupational performance (employment, absenteeism and presenteeism) among chronic obstructive pulmonary disease patients in employment (work package 3, manuscript in preparation)	26
<i>Rationale</i>	26
<i>What we did</i>	26
<i>What we found</i>	27
<i>Strengths and limitations</i>	27
Objective (iii): to assess the feasibility and benefits of offering formal occupational health assessment and subsequent recommendations aimed at improving work-based indices to people with chronic obstructive pulmonary disease in employment (work package 3, published PhD thesis)	27
<i>Rationale</i>	27
<i>What we did</i>	28
<i>What we found</i>	28
<i>Strengths and limitations</i>	28
Additional outputs and published analyses related to work package objectives	28
Patient and public involvement	29
<i>Patient advisory group</i>	29
<i>Multistory</i>	29
Conclusions and research recommendations	30
<i>Screening for undiagnosed chronic obstructive pulmonary disease</i>	30
<i>Multidimensional prognostic model for chronic obstructive pulmonary disease</i>	31
<i>Occupational outcomes in chronic obstructive pulmonary disease</i>	32
Summary of research recommendations	32
<i>Screening</i>	32
<i>Prognosis</i>	32
<i>Work-related impacts</i>	33
Acknowledgements	35
References	39
Appendix 1 List of publications arising from programme, with full-text links	49
Appendix 2 Screening questionnaire for TargetCOPD trial	59
Appendix 3 Baseline questionnaires for Birmingham chronic obstructive pulmonary disease cohort participants	65
Appendix 4 Development of the Birmingham Lung Improvement Studies prognostic score for chronic obstructive pulmonary disease patients in primary care: data from the Birmingham chronic obstructive pulmonary disease cohort	123

List of tables

TABLE 1 Clinical management during the 2-year follow-up of participants with EHR data who were case-found vs. those clinically diagnosed through usual care	10
TABLE 2 Cohort questionnaire items and response rate at different follow-up points	17

List of figures

FIGURE 1 Overview of the programme of work	2
FIGURE 2 Flow of participants contributing to analyses for this study	10
FIGURE 3 Flow chart of patient recruitment and assessment for the Birmingham COPD cohort study	16
FIGURE 4 Cumulative number of cohort participants recruited and having baseline assessments by month	17

List of abbreviations

ADO	age, dyspnoea, airflow obstruction	IQR	interquartile range
ATC	American Thoracic Society BLISS Birmingham Lung Improvement Studies	IRR	incidence rate ratio
BMI	body mass index	LLN	lower limit of normal
BODE	body mass index, airflow obstruction, dyspnoea, and exercise	MCID	minimal clinically important difference
CAT	COPD Assessment Test	MRC	Medical Research Council
CI	confidence interval	NICE	National Institute for Health and Care Excellence
COPD	chronic obstructive pulmonary disease	OH	occupational health
EHR	electronic health record	OR	odds ratio
EQ-5D	EuroQol-5 dimensions	PA	physical activity
ERS	European Respiratory Society	PAG	patient advisory group
FEV ₁	forced expiratory volume in 1 second	PRP	pulmonary rehabilitation programme
FVC	forced vital capacity	QALY	quality-adjusted life-year
HES	Hospital Episode Statistics	QOF	Quality and Outcomes Framework
HR	hazard ratio	RCGP	Royal College of General Practitioners
HRQoL	health-related quality of life	RCT	randomised controlled trial
HSE	Health Survey for England	SD	standard deviation
ICER	incremental cost-effectiveness ratio	USPSTF	US Preventive Services Task Force
IMD	index of multiple deprivation	VGDF	vapours, gases, dusts or fumes
		WP	work package

Plain English summary

Chronic obstructive pulmonary disease is an important lung disease, affecting around 10% of adults worldwide. Each year in the UK, it accounts for 1.4 million general practitioner consultations, 1 million hospital bed-days and around 24 million lost working days. However, at least half of those with chronic obstructive pulmonary disease are unaware of their diagnosis and these people may not receive early treatment. Before our research there was uncertainty about (1) how to best identify these missing patients, (2) whether or not early identification would benefit patients, (3) how chronic obstructive pulmonary disease progresses, (4) what characteristics (other than smoking) affect risk of hospital admission or early death and (5) what aspects influence ability to work in people with chronic obstructive pulmonary disease.

We found that if general practitioners offered screening to smokers aged over 40 years then they could identify seven times as many people with chronic obstructive pulmonary disease than they do currently. However, although these patients could potentially benefit from therapies, the health system was not set up to support doctors to provide all the recommended treatments. Our economic model suggested that screening was worthwhile for detecting undiagnosed chronic obstructive pulmonary disease. However, after 4 years we found that screening did not reduce the risk of hospital admissions or death.

We also followed up around 2000 people with chronic obstructive pulmonary disease to see which features were linked with the risk of hospital admission with a lung problem. Through this we developed a tool that could measure an individual's chronic obstructive pulmonary disease severity. This has the potential to allow doctors to make more appropriate patient management decisions, but it needs more testing.

Finally, we examined which attributes (related to the patient, their lung problem or their workplace) affected people's ability to work. We found that people who are more breathless or exposed to inhaled hazards may have poorer work performance. However, because few patients in the study were in paid employment, we cannot draw firm conclusions.

Scientific summary

Background

At least half of people with chronic obstructive pulmonary disease are undiagnosed, but the best approach for identifying them is not established. Furthermore, screening is not recommended because it is not yet known if it leads to clinical benefits.

There is increasing recognition that chronic obstructive pulmonary disease is heterogeneous, and, although a number of prognostic models have been developed, most prognostic models include people with more severe disease within secondary care. It is not known which combination of phenotypic characteristics best predict prognosis in the larger primary care chronic obstructive pulmonary disease population, particularly in relation to respiratory hospitalisations.

Effective treatment for those with mild chronic obstructive pulmonary disease is limited. Physical activity promotion is a potential intervention, but its acceptability to primary care chronic obstructive pulmonary disease patients is unknown.

A substantial proportion of chronic obstructive pulmonary disease patients are of working age. Although there is some evidence that they have poorer employment history and work productivity, the main factors that are associated with these outcomes have not to our knowledge been previously studied.

The aim of this programme was to address the above uncertainties.

Objectives

Work package 1

- Ascertain the clinical effectiveness and cost-effectiveness of targeted case-finding (opportunistic or active) compared with routine care.
- Develop a Markov model to compare the cost-effectiveness of systematic case-finding with current practice.
- Explore the views of patients and primary care staff on chronic obstructive pulmonary disease case-finding.
- Describe the clinical management of screen-detected chronic obstructive pulmonary disease patients in primary care.
- Assess the long-term effectiveness of chronic obstructive pulmonary disease case-finding on respiratory hospitalisations and mortality.
- Compare outcomes among screen-detected chronic obstructive pulmonary disease patients who were adequately managed by their general practitioner with those among patients who were not.

Work package 2

- Recruit a primary care cohort of 2000 new and existing chronic obstructive pulmonary disease patients.
- Test the validity of existing chronic obstructive pulmonary disease prognostic models in a primary care chronic obstructive pulmonary disease population.
- Develop a prognostic model (BLISS index) to predict respiratory hospitalisations suitable for a primary care population.
- Explore the barriers to and facilitators of physical activity participation among people with chronic obstructive pulmonary disease.

Work package 3

- Examine factors associated with occupational performance [employment, absenteeism and presenteeism (working while unwell)] among chronic obstructive pulmonary disease patients of working age.
- Examine how disease progression is associated with occupational performance.
- Assess the feasibility of offering occupational health assessment with recommendations to people with chronic obstructive pulmonary disease.

Methods

Work package 1: TargetCOPD cluster randomised controlled trial

Fifty-four general practices were randomly assigned to either targeted case-finding or routine care. Eligible patients were people who had smoked, were aged 40–79 years and did not have a previous chronic obstructive pulmonary disease diagnosis. Those in the targeted arm were further randomly assigned to receive a symptom screening questionnaire either at any general practitioner visit (opportunistic) or by post (active). Respondents reporting relevant respiratory symptoms were invited for diagnostic post-bronchodilator spirometry.

Primary outcomes were percentage of the eligible population diagnosed with chronic obstructive pulmonary disease within 1 year (yield) and cost per new chronic obstructive pulmonary disease diagnosis using trial data.

At 4–5 years' follow-up, data on mortality and hospitalisations were obtained from NHS Digital for all eligible patients, and case-found chronic obstructive pulmonary disease patients were invited to complete a health questionnaire to report on their health-related quality of life as well as treatments received for chronic obstructive pulmonary disease. For case-found patients, we also obtained data from electronic health records on whether or not they had been added to the practice's Quality and Outcomes Framework chronic obstructive pulmonary disease register within 12 months and whether or not they had been prescribed a range of chronic obstructive pulmonary disease treatments.

Cox proportional hazards models adjusted for potential confounding factors were used to model the time to clinical outcomes (i.e. death, first respiratory hospital admission) in the intervention and routine arms. Time to event was censored at death (for admission) or study end date if no event occurred.

For case-found patients, we used logistic and Poisson regression to compare mortality, hospitalisation and health-related quality of life among those who were and those who were not added to the chronic obstructive pulmonary disease register, adjusting for baseline values and relevant confounders.

Data from the trial and our cohort study (work package 2) as well as from the published literature were used to develop a Markov decision-analytic model to compare the cost-effectiveness of a 3-yearly case-finding programme aimed at people who have smoked aged > 50 years with current practice, taking a health service perspective.

We interviewed patients who had been invited for screening and primary care staff in targeted case-finding practices to explore their views on screening.

Work package 2: Birmingham primary care chronic obstructive pulmonary disease cohort

Patients aged ≥ 40 years with previously diagnosed chronic obstructive pulmonary disease from 71 practices, as well as those reporting chronic respiratory symptoms as part of the TargetCOPD trial, were invited to join the cohort study. Participants underwent detailed baseline assessment, were followed up with 6-monthly questionnaires and underwent a final assessment at ≈ 3 years.

Using data from those with chronic obstructive pulmonary disease in the cohort, linked to mortality data obtained from NHS Digital, we sought to validate the ADO (age, dyspnoea, airflow obstruction) prognostic score. This was shown to be the most discriminatory among current indices in predicting mortality in a recent review. Discrimination was calculated using the c-statistic. Calibration was assessed by comparing predicted with actual probability of mortality.

To develop a new index to predict respiratory admissions, we considered 23 candidate variables identified from the literature and by a clinician stakeholder group. Self-reported and clinical data from cohort patients were linked to hospitalisation data obtained through NHS Digital. The primary outcome was the record of at least one respiratory admission within 2 years of cohort entry. The model was developed using backward elimination ($p < 0.157$ for retention). Fractional polynomials were considered and multiple imputation using chained equations was used for missing data. Discrimination and calibration were assessed. Bootstrapping was used for internal validation and the optimum-adjusted performance statistics were estimated.

A purposive sample of 26 cohort patients with a range of chronic obstructive pulmonary disease severity participated in one of four focus groups to explore perceived barriers to and facilitators of physical activity engagement, using the social cognitive theory framework. Thematic analysis identified key concepts related to the patients' self-efficacy beliefs.

Work package 3: occupational performance and outcomes in chronic obstructive pulmonary disease

Using baseline data of cohort participants who were of working age, we compared the sociodemographic, clinical and occupational characteristics of people who were in paid employment with those of people who were not. Among those in paid employment, we examined characteristics associated with absenteeism (self-report over previous 12 months) and presenteeism (Stanford Presenteeism Scale).

Longitudinal multivariable regression analyses, adjusting for clinical, sociodemographic, occupational and labour market factors among participants in paid employment, were conducted to examine the effects of disease progression [forced expiratory volume in 1 second decline, respiratory hospitalisations (exacerbations), increase in Medical Research Council dyspnoea score, worsening Chronic Obstructive Pulmonary Disease Assessment Test score] on employment, absenteeism and presenteeism.

Cohort participants who were in paid employment at baseline were invited for a tailored occupational health assessment to explore and identify workplace factors that might contribute to their work performance and to recommend appropriate modifications. Participants' self-management practices were also assessed. Recommendations were sent to the participant and, with their permission, to their general practitioner and employer. We examined acceptability and feasibility of the intervention.

Results

Work package 1

Effects of case-finding on yield

A total of 74,818 patients took part. Very few new cases of chronic obstructive pulmonary disease were diagnosed in routine practice. The yield from targeted case-finding was significantly higher (adjusted odds ratio 7.45, 95% confidence interval 4.80 to 11.55) and active case-finding was more clinically effective (adjusted odds ratio 2.34, 95% confidence interval 2.06 to 2.66) and more cost-effective than the opportunistic-only approach (£333 vs. £376 per case detected, respectively).

Decision-analytic model of cost-effectiveness of case-finding

Our model predicted that the incremental cost-effectiveness ratio of a systematic 3-year case-finding programme compared with routine care was £16,596 per additional quality-adjusted life-year gained if assumptions hold, giving this a high probability of being cost-effective using the UK willingness-to-pay threshold of £20,000 per quality-adjusted life-year.

Stakeholder views on case-finding

Both patients and primary care staff generally considered screening to be valuable. Patients highlighted the presence of symptoms and convenience of the screening process as factors promoting screening attendance. Better support from secondary care, an increase in specialist chronic obstructive pulmonary disease nurses and better community respiratory service provision would support primary care staff in undertaking case-finding. Patient barriers to screening attendance included psychological and practical factors, such as time, availability and perceived lack of general practitioner time. Primary care staff had concerns around lack of resource for increasing workload and potential harm from overdiagnosis.

Management of case-found patients

A year after case-finding, approximately one-fifth of case-found patients but > 90% of routinely diagnosed patients had been added to a chronic obstructive pulmonary disease register. Patients who had been added to a chronic obstructive pulmonary disease register were significantly more likely to receive appropriate chronic obstructive pulmonary disease-related care (more than five items of clinical assessment and/or management) than those who had not been added to a register. However, even among those on the register, fewer than one-quarter of eligible patients had ever been referred to pulmonary rehabilitation and a significant proportion of smokers had not received smoking cessation support.

Effectiveness of case-finding on clinical outcomes

Over a mean follow-up of 4.3 years, 4.8% (1557/32,743) of patients in the case-finding arm and 4.5% (1899/41,950) in the routine arm had a respiratory hospitalisation (adjusted hazard ratio 1.04, 95% confidence interval 0.73 to 1.47). The corresponding hazard ratio for mortality was 1.15 (95% confidence interval 0.82 to 1.61), suggesting that, overall, there was no significant difference in risk of hospitalisation and mortality between case-found and routine care arms and there was no noteworthy difference in outcomes between those in the two case-finding intervention arms. Among the case-found patients, when comparing those who were and those who were not on the chronic obstructive pulmonary disease register, there was no statistically significant difference in clinical outcomes or in EuroQol-5 Dimensions scores, although the Chronic Obstructive Pulmonary Disease Assessment Test score was higher in those on the chronic obstructive pulmonary disease register (mean difference 2.317, 95% confidence interval 0.481 to 4.153), indicating greater impact of chronic obstructive pulmonary disease on their health-related quality of life.

Work package 2

Birmingham chronic obstructive pulmonary disease cohort

Data on 2250 patients (97.8%) were available over 3 years. Six-monthly questionnaires were completed by approximately two-thirds of patients. Over the period of follow-up (minimum 1.8 years, maximum 3.8 years), 382 patients (17%) had at least one respiratory hospital admission and 124 patients died.

Validation of age, dyspnoea, airflow obstruction prognostic score

Valid data were available for 1701 chronic obstructive pulmonary disease patients with airflow obstruction (309 case-found patients). Age, dyspnoea, airflow obstruction prognostic scores discriminated 3-year mortality accurately (c -statistic 0.73, 95% confidence interval 0.67 to 0.79), with similar discriminatory ability for 2- and 1-year mortality (c -statistic 0.72, 95% confidence interval 0.67 to 0.77 and 0.73 and 95% confidence interval 0.66 to 0.80, respectively). However, there was some overprediction, which was more pronounced at 1- and 2-year mortality time points (calibration

slopes 0.96, 0.80 and 0.79 for 3- 2- and 1-year mortality, respectively) and in those with higher baseline age, dyspnoea, airflow obstruction prognostic scores.

Development of the Birmingham Lung Improvement StudieS prognostic index

Among 1564 previously diagnosed and 330 case-found patients, 253 (13%) had a respiratory admission within 2 years (367 had a respiratory admission over median follow-up of 3 years). Out of 23 candidate variables, six were retained in the final developed model: age, Chronic Obstructive Pulmonary Disease Assessment Test score, respiratory admissions in the previous 12 months, body mass index, diabetes and forced expiratory volume in 1 second percentage predicted. After adjustment for optimism, the primary model performed well in discriminating between those with and without 2-year respiratory admissions (*c*-statistic 0.75, 95% confidence interval 0.72 to 0.79).

Barriers to and facilitators of physical activity engagement

Several barriers to and facilitators of engagement with physical activity, closely related to self-efficacy beliefs and symptom severity, were identified. Barriers were health related, psychological, attitudinal and motivational. Self-regulation (e.g. keeping a routine), self-efficacy (sense of achievement), enjoyment and social aspects of physical activity motivated participation.

Work package 3

Factors associated with occupational outcomes

Among 608 cohort participants of working age, 248 (40.8%) were in paid employment. Older age (odds ratio 0.28, 95% confidence interval 0.12 to 0.65), lower educational level (odds ratio 0.43, 95% confidence interval 0.19 to 0.97), poorer BODE (body mass index, airflow obstruction, dyspnoea, and exercise) prognostic score (odds ratio 0.10, 95% confidence interval 0.03 to 0.33) and history of high occupational exposure to vapours, gases, dusts or fumes (odds ratio 0.32, 95% confidence interval 0.12 to 0.85) were associated with a lower probability of being employed. Of those in paid employment, higher levels of dyspnoea were associated with both absenteeism and presenteeism (*p*-trend < 0.01). Additionally, occupational vapours, gases, dusts or fumes exposure was associated with presenteeism (*p*-trend < 0.01).

Follow-up data were available for 174 of those in paid employment at baseline. Over a mean follow-up of 25.8 months, 144 (82.8%) participants remained employed. The point estimate suggested an inverse association between increasing respiratory hospital admissions and probability of remaining in work (odds ratio 0.32, 95% confidence interval 0.09 to 1.14; *p* = 0.08), although wide confidence intervals suggest that further research is needed.

Prospective absenteeism data were available for 113 participants (mean follow-up of 19.5 months). Worsening breathlessness (incidence rate ratio 3.06, 95% confidence interval 1.29 to 7.26; *p* = 0.01) and increasing respiratory hospital admissions (incidence rate ratio 2.01, 95% confidence interval 1.09 to 3.69; *p* = 0.03) were associated with increased sickness absence. Follow-up presenteeism data were available for 163 participants (86.2%), where 43 (26.4%) had worsening presenteeism. This was significantly associated with worsening Chronic Obstructive Pulmonary Disease Assessment Test score (odds ratio 5.74, 95% confidence interval 1.18 to 27.83; *p* = 0.03) and there was some evidence of association with worsening dyspnoea.

Occupational health feasibility study

Only 35 (11.3%) of the eligible patients agreed to take part in the occupational health study. Of these, 80.0% received at least one occupational health recommendation and all received self-management recommendations. However, only 37.3% of recommendations were reported as implementable. The very low uptake rates for the intervention and low implementation of recommendations suggests that, in its current format, the intervention is not feasible.

Conclusions

Despite screening resulting in higher yield of undiagnosed cases of chronic obstructive pulmonary disease and promising results from our health economic model, we did not find evidence of clinical benefit at 4 years' trial follow-up. The poor clinical management of chronic obstructive pulmonary disease generally, and low addition of case-found patients to the practice chronic obstructive pulmonary disease register, may explain the findings. The benefit of current treatments in case-found patients remains unknown.

For a screening programme to be implemented and have high uptake, it is important to raise patient awareness of chronic obstructive pulmonary disease risk factors and symptoms and provide training and additional resources for primary care. In particular, it is important to ensure that management pathways for diagnosed chronic obstructive pulmonary disease patients are optimised before further cases are identified.

We have developed a new index, using data from people with chronic obstructive pulmonary disease in a UK primary care setting, that has good discrimination performance in predicting respiratory hospitalisations. This needs external validation and examination of its impact on care and outcomes. We confirmed that the age, dyspnoea, airflow obstruction score is discriminatory for predicting mortality in a primary care population.

Among people with chronic obstructive pulmonary disease who are of working age, having greater breathlessness, a greater number of respiratory admissions and greater occupational exposure to vapours, gases, dusts or fumes are associated with poorer work productivity. Although our occupational health intervention was not feasible, modifiable workplace adaptations and self-management actions were identified for almost all participants, suggesting possible benefit from such assessments in a different context.

Recommendations for further research

- Development and evaluation of interventions to improve management of chronic obstructive pulmonary disease in primary care, including pathways to manage case-found chronic obstructive pulmonary disease.
- Evaluation of existing interventions in case-found chronic obstructive pulmonary disease.
- External validation of the BLISS index in new data.
- Evaluation of impact of using the BLISS index to guide patient management.
- Development and evaluation of interventions to reduce dyspnoea and vapours, gases, dusts or fumes exposure on occupational outcomes in people with chronic obstructive pulmonary disease.

Trial registration

This trial is registered as ISRCTN14930255.

Funding

This project was funded by the National Institute for Health Research (NIHR) Programme Grants for Applied Research programme and will be published in full in *Programme Grants for Applied Research*; Vol. 9, No. 13. See the NIHR Journals Library website for further project information.

SYNOPSIS

Background

Chronic obstructive pulmonary disease (COPD) is a chronic progressive respiratory condition with an estimated worldwide prevalence of 9.2¹–11.7%² in adults aged ≥ 30 years. However, at least half of all people with COPD (depending on the diagnostic criteria) remain undiagnosed, representing a large number with potentially unmet need.^{3,4} COPD is defined by the presence of airflow obstruction among those with relevant risk factors but there is increasing recognition that the disease is heterogeneous, with different causative factors, phenotypic characteristics and varying prognosis.^{5,6} A substantial proportion of those with COPD are of working age, and there is some evidence that they have poorer employment history,⁷ higher rates of sickness absence⁸ and poorer work performance [because of presenteeism (working while unwell)]⁹ compared with the general population. In the UK, COPD is estimated to cost the NHS around £1.5B (2011 costs),^{10,11} with total costs (including societal and intangible costs) nearing £48.5B (2014 costs)¹² per year. This compares with estimates of around US\$49.9B in the USA (2010 prices)¹³ and €48.4B in the European Union (2011 prices).¹⁴

At the time of developing this proposal in 2009/10, there was much uncertainty about the natural history of COPD,^{5,15} how to approach early identification of patients^{16,17} and what interventions were effective for early-stage disease. During the conduct of the programme, both the UK National Screening Committee and the US Preventive Services Task Force (USPSTF) highlighted the lack of randomised controlled trial (RCT) evidence that showed that screening for COPD is beneficial. We therefore sought a variation to our contract to undertake additional work to that proposed in the original funded application: to follow up trial participants to examine the impact of screening on clinical outcomes. There was also little information on the impact that having COPD has on work performance and occupation. Furthermore, most of the previous research to explore prognosis and natural history of COPD were based on people with COPD recruited through secondary care and specialised settings, rather than within primary care.^{18–20} The overall aim of this programme was therefore to recruit a unique UK primary care COPD cohort to address some of these uncertainties and, as a platform for future research, to test novel health service interventions.

Overview of research programme

The programme consisted of three inter-related work packages (WPs), each addressing several research questions. *Figure 1* provides an overview of the linked WPs in the programme, which are briefly described below. Each WP is then described in more detail, outlining the rationale, the research questions addressed and a summary of the findings and outputs linked to the original programme objectives. A full list of publications arising from our programme is available in *Appendix 1*.

Work package 1: clinical trial to evaluate case-finding; TargetCOPD trial

The aim of this WP was to ascertain the most clinically effective and cost-effective approach to identifying undiagnosed COPD. Initially, this was considered in terms of yield (WP1i), but with additional follow-up (in a variation to the contract) in terms of clinical outcomes (WP1v and vi). A Markov model was also developed to estimate the long-term cost-effectiveness of a systematic screening programme for undiagnosed COPD. Finally, we explored the views of patients on the process and outcomes of case-finding and the perspective of staff in primary care on the concept of case-finding and perceived implications for their practice.

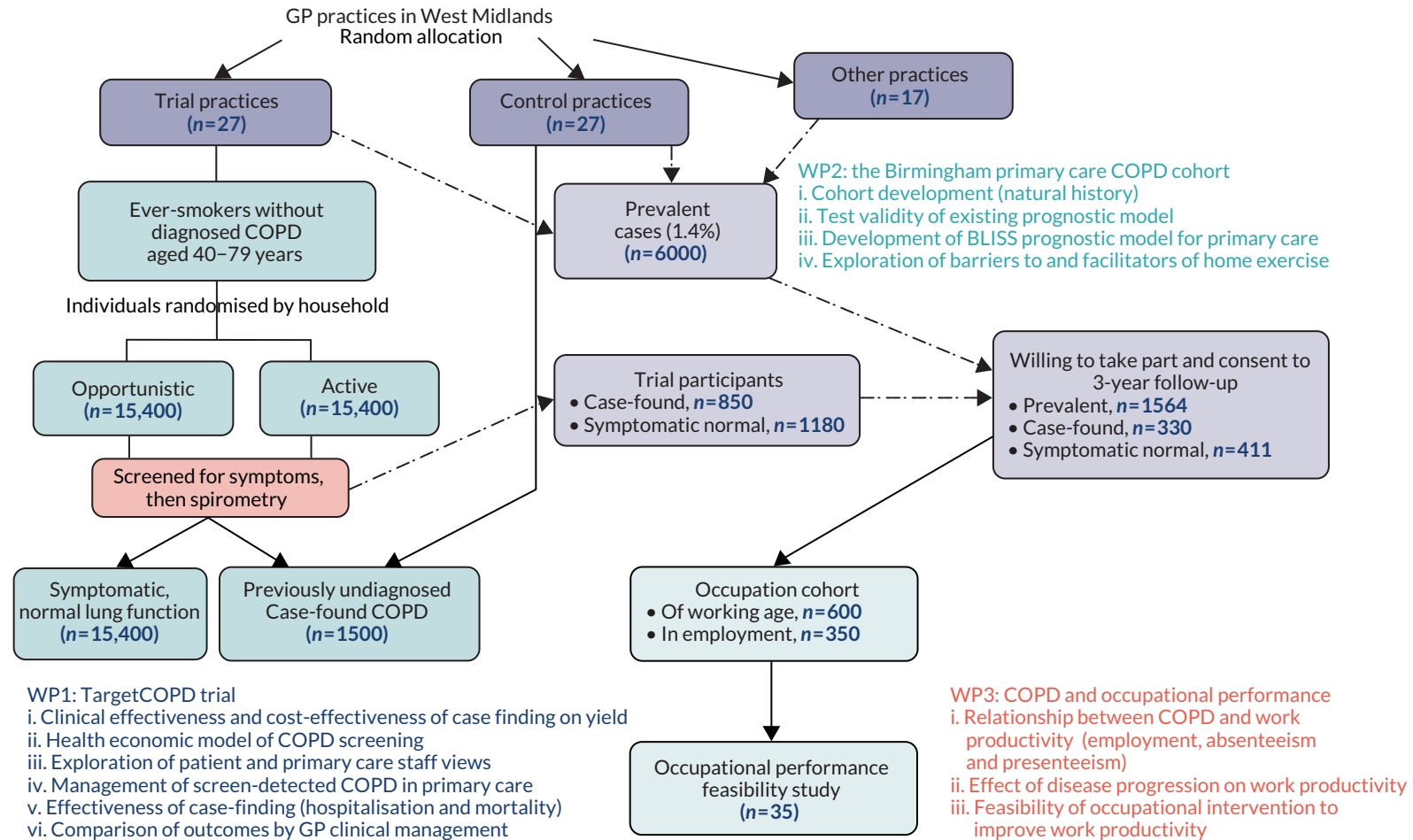


FIGURE 1 Overview of the programme of work. BLISS, Birmingham Lung Improvement Studies.

The objectives were to:

- ascertain the clinical effectiveness and cost-effectiveness of targeted case-finding (opportunistic or active) compared with routine care
- develop a Markov model to compare the cost-effectiveness of systematic case-finding with current practice
- explore the views of patients and primary care staff on COPD case-finding
- describe the clinical management of screen-detected COPD patients in primary care
- assess the long-term effectiveness of COPD case-finding on respiratory hospitalisations and mortality
- compare outcomes among screen-detected COPD patients who were adequately managed by their general practitioner (GP) with those among patients who were not.

Work package 2: Birmingham primary care chronic obstructive pulmonary disease cohort

The aim of this WP was to develop a cohort of more than 2000 people with COPD who would be representative of those in a primary care setting, including more people with mild/moderate disease than included in previous cohorts. Participants were recruited from COPD registers in general practices as well as from participants in the TargetCOPD trial in WP1. This included those who were identified through case-finding and those who took part in the case-finding trial and reported respiratory symptoms but did not have COPD based on spirometry.

The participants were followed up every 6 months for around 3 years (2012–16) and their data were linked to routine data on hospitalisation and mortality obtained from NHS Digital. We used these data to externally validate an established prognostic model [the age, dyspnoea, airflow obstruction (ADO) prognostic score] in predicting mortality. In addition, we developed a new prognostic model [the Birmingham Lung Improvement StudieS (BLISS) index] to predict the risk of respiratory hospitalisation in this primary care population.

A sample of 26 cohort participants were also invited to attend focus groups to explore barriers to and facilitators of undertaking physical activity (PA), which is one of the most important components of treatment for people with COPD.

The establishment of the cohort also provides an opportunity for testing novel interventions in future.

The objectives were to:

- recruit a primary care cohort of 2000 new and existing COPD patients
- test the validity of existing COPD prognostic models in a primary care COPD population
- develop a prognostic model (BLISS index) to predict respiratory hospitalisations suitable for a primary care population
- explore barriers to and facilitators of PA participation among people with COPD.

Work package 3: chronic obstructive pulmonary disease and occupational performance

The aims of this WP were to (1) examine the relationship between clinical characteristics and severity of COPD and occupational outcomes, including employment, work absenteeism and presenteeism (working while unwell); (2) examine whether or not disease progression over time is associated with occupational outcomes; and (3) assess the feasibility and benefits of offering formal occupational health (OH) assessment and subsequent recommendations aimed at improving work-based indices. Participants in this WP were a subsample of the larger cohort recruited in WP2.

SYNOPSIS

The objectives were to:

- examine factors associated with occupational performance (employment, absenteeism and presenteeism) among COPD patients of working age
- examine how disease progression (lung function decline, exacerbation) over time is associated with occupational performance (employment, absenteeism and presenteeism) among COPD patients in employment
- assess the feasibility of offering OH assessment with recommendations to people with COPD.

Work package 1: clinical trial to evaluate case-finding – TargetCOPD trial

Objective (i): to ascertain the clinical effectiveness and cost-effectiveness of targeted case-finding (opportunistic or active) compared with routine primary care (work package 1i, published trial report)²¹

Parts of this section are based on Jordan *et al.*²¹ Reprinted from *The Lancet Respiratory Medicine*, Vol. 4, Rachel E Jordan, Peymané Adab, Alice Sitch, Alexandra Enocson, Deirdre Blissett, Sue Jowett, *et al.*, Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial, pp. 720–30, Copyright 2016, with permission from Elsevier.

Rationale

Several reports from the UK government and health charities^{22,23} have highlighted the burden of COPD, the extent of underdiagnosis and the variation in access to and participation in relevant services. The Department of Health and Social Care published an outcomes strategy for people with COPD in 2011 that recommended opportunist and the systematic case-finding to minimise late diagnosis.²² However, the most clinically effective and cost-effective approach for identifying undiagnosed cases was not known. Although some published studies reported the yield from either active^{24–26} or opportunistic^{27–29} approaches to case-finding using spirometry, these were limited because of a lack of comparison groups, the restricted number and range of participants, a lack of follow-up and different target populations (e.g. specific age groups; all current smokers or people who have smoked; whether or not symptoms were considered prior to spirometry). Furthermore, general population screening using spirometry was not recommended¹⁶ because it would identify many people without clinically important disease, for whom there is little evidence of effective interventions.³⁰ We therefore sought to evaluate different approaches to case-finding for undiagnosed COPD, focusing on yield and cost-effectiveness (from a health-care perspective). To our knowledge, this was the first major trial to compare different targeted recruitment approaches with case-finding with routine care.

What we did

We recruited 54 GP practices across the West Midlands (10 August 2012–22 June 2013) to take part in the 12-month trial and randomised these clusters to case-finding or to continue with routine care. All patients on the practice registers aged 40–79 years who had no existing diagnosis of COPD and had ever smoked (based on GP electronic records) were eligible for and included in the trial. Using a computer-generated randomisation sequence, we randomised practices (balanced on practice characteristics) and in the intervention case-finding arm we randomised individual households of patients to receive one of two approaches to case-finding: opportunistic (offered screening opportunistically when they visited the practice for any reason) or active (additionally offered screening through a postal invitation). Screening was carried out in two stages, with an initial questionnaire (see *Appendix 2*) followed by an invitation to attend for diagnostic spirometry for those who reported relevant chronic respiratory symptoms. Our study case definition of 1-year incident COPD was either (1) a new diagnosis of COPD by the GP (based on new entry on practice COPD register) or (2) the presence of airflow obstruction on screening [defined as forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) < 0.7 post bronchodilator, in line with recommendations from the guidelines³¹ produced by the National Institute for Health and Care Excellence (NICE)] in patients with chronic respiratory symptoms. Sample sizes were based on estimates from our published model (see published paper²¹ for full details) and required 27,768 patients per group. Primary outcomes were analysed using appropriate regression analyses adjusted for practice-level deprivation, ethnicity and age. The active versus opportunistic comparison

required logistic regression with fixed effects and the targeted versus routine comparison required multilevel models with random effects. We undertook a within-trial cost-effectiveness analysis to calculate the cost per additional case detected of both strategies versus routine care, and we undertook a detailed cost analysis of the screening processes using standard NHS^{32,33} and trial-specific costs³⁴ (2013 prices), including set-up costs and training costs. Equipment and training costs were amortised over 3–5 years using a discount rate of 3.5%. Sensitivity analyses considered patient costs, alternative case-finding scenarios and models of care (GP, community or secondary care led).

What we found

A flow diagram of participants is available in the published paper.²¹ We found that very few new cases of COPD were diagnosed in the routine care practices ($n = 337$; 0.8%). The odds of finding new cases were seven times higher using the targeted approach than with routine care [$n = 1278$ (4%); adjusted odds ratio (OR) 7.45, 95% confidence interval (CI) 4.80 to 11.55; $p < 0.0001$], and active case-finding (combining opportunistic and active postal invitation to screening) was twice as effective as opportunistic-only [$n = 822$ (5%) vs. $n = 370$ (2%); adjusted OR 2.34, 95% CI 2.06 to 2.66; $p < 0.0001$]. Active case-finding may also be more cost-effective than the opportunistic approach (£333 vs. £376 per additional case detected, respectively). The incremental cost-effectiveness ratio (ICER) for active case-finding was £573 per additional case detected compared with opportunistic case-finding. Sensitivity analyses made little difference, although a secondary care-led service was more expensive.

Strengths and limitations

To our knowledge, this was the first RCT to compare yield of undiagnosed COPD from a comparison of different screening approaches with routine practice and to estimate their cost-effectiveness. However, the efficiency of screening could have been improved by using different screening tests, or pre-screening algorithms applied to electronic health records (EHRs) to target screening invitations to those at highest risk. Even with the most intensive screening approach, only 38% of those invited for screening responded, and not all those who responded and had symptoms attended for diagnostic spirometry. Further research should focus on how to maximise screening coverage and uptake and improve the efficiency of the screening process.

Objective (ii): to develop a model (using Markov decision analysis) to compare the cost-effectiveness of a systematic case-finding programme with current practice (work package 1ii, published)³⁵

Rationale

The TargetCOPD trial confirmed that active approaches to screening result in a higher proportion of undiagnosed COPD patients being identified compared with routine care. People with screen-detected COPD are expected to benefit from treatment resulting in improved quality of life, increased survival and reduction in hospital admissions. To provide data for policy-makers to consider the longer term benefits of screening for COPD in relation to investment in other health services, a cost-utility model is needed. Published economic evaluations in COPD have primarily considered interventions for the disease rather than for those who are screen detected,³⁶ and others have concentrated on the costs of COPD in burden of illness studies.³⁷ No trial-based economic evaluation had considered case-finding. NICE guidelines³⁸ included a simple decision tree-based modelling to determine the cost-effectiveness of opportunistic case-finding among people aged > 35 years who have smoked and have a chronic cough. However, the model was simplistic and included many assumptions for which evidence was limited. We developed a model-based economic evaluation of the long-term costs and benefits of screening for undiagnosed COPD.

What we did

We used costs (using 2015 prices³⁹) and outcome data from the TargetCOPD trial, in combination with the best available published data, and additional information from our linked Birmingham COPD cohort study (WP2) to develop a Markov decision-analytic model to address this objective. The model

compared the cost-effectiveness of a 3-yearly systematic case-finding programme aimed at people aged > 50 years who have smoked with current practice because the yield of new cases was very small in younger age groups. The model had a time cycle of 3 months, which was short enough to capture important COPD-related events, and a time horizon of 50 years, assuming a maximum age of 100 years. Patient-level data on case-finding pathways were obtained from our TargetCOPD RCT. The model outcome was cost per quality-adjusted life-year (QALY) gained, from a health service perspective. Discounting was applied to costs and outcomes at 3.5%. Multiple one-way sensitivity analyses assessed what impact modification of key parameters had on the results. We considered varying the starting age, screening interval and time horizon as well as the screening processes (questionnaire response, spirometry attendance rate), treatment initiation rates and effectiveness of treatments.

What we found

We estimated the ICER of systematic case-finding compared with routine care to be £16,596 per additional QALY gained. Using the commonly used willingness-to-pay threshold in the UK (£20,000 per QALY), we estimated there was 78% probability of cost-effectiveness. The estimate was robust to sensitivity analyses, with the main cost-driver being uptake of screening. The most cost-effective age to begin screening was around 60 years. Better ascertainment of treatment effectiveness will help improve precision but, using the best current estimates from the literature,^{40,41} screening is likely to be cost-effective provided that at least 12% respond to a screening questionnaire, > 26% attend spirometry and > 8% of screen-detected patients are adequately treated and managed.

Strengths and limitations

To our knowledge, this is the first economic model to evaluate the long-term cost-effectiveness of a COPD case-finding strategy, using contemporaneous data sources to inform estimates and using multiple sensitivity analyses to test the robustness of the model. However, the validity of some of the assumptions underlying the model is unknown. In particular, there is uncertainty around the effect of treatment on progression and the natural history of COPD. Future research should refine the model based on data from studies that provide more accurate estimates of effectiveness and consider additional costs, such as those to the health service, of pathways to deal with a larger number of identified cases.

Objective (iii): to explore the views of (a) patients invited to take part in case-finding, in terms of the process and outcomes (work package 1iii, published),⁴² and (b) primary care staff, in relation to case-finding (work package 1iii, published)⁴³

Rationale

Although there has been much research examining the yield from different case-finding activities, few previous studies have examined other aspects related to the development of a screening programme. One important aspect is the acceptability of screening and understanding the perspective of both patients and those who provide screening. We undertook two studies: one to explore the views of patients who had been invited for screening as part of the TargetCOPD trial, about the screening process and outcomes, and another to understand the process from the perspective of primary care staff who would manage those who are case-found.

What we did

For the patient perspective, we invited for interview people who had been invited for screening in either the active or opportunistic arm as part of the TargetCOPD trial (i.e. adults aged ≥ 40 years with a smoking history who had been considered eligible for the trial by their GP). We invited four groups of patients: those who (1) were invited and consented to take part in screening, (2) were invited and declined, (3) attended screening but did not have COPD and (4) attended and had abnormal lung function suggesting COPD. We sought their views on the screening process and their reflections on the outcomes of screening.

For the primary care staff perspective, we invited 20 staff, including GPs, nurses and managers in practices that had taken part in the TargetCOPD trial. Participants were invited to share their views on COPD case-finding, including their perceptions of the benefits, harms, and barriers to and facilitators of implementing a screening programme in primary care.

For both studies, interviews were transcribed and analysed using the framework approach.

What we found

Forty-three patients and 20 health-care staff were interviewed. Patients generally considered screening to be a good thing, and the presence of symptoms on prompting facilitated their attendance. The importance of ensuring that the screening process is convenient was highlighted, and patients worried that GPs did not have the time to follow up after screening.

Barriers to attending screening included psychological and practical factors. The former related to denial and failure to recognise symptoms, fear of the 'test' and perceiving lung disease as less important within the hierarchy of their health problems. Practical barriers included lack of time, inability to access GP appointments and having caring and other responsibilities that were considered more important.

Among primary care staff, although they also generally supported screening for undiagnosed COPD, they also commented on concerns around potential negative consequences, including an increase in workload for GPs and overdiagnosis in patients. Some commented that, currently, diagnosed patients were not being adequately treated. Perceived barriers to implementing screening included lack of resources and limited access to diagnostic services. However, potential solutions, including better support from secondary care, an increase in specialist COPD nurses and better community respiratory service provision, were also discussed. Poor knowledge of COPD in terms of recognising symptoms and how to manage those with the disease was also highlighted as a problem that needs to be addressed.

For a screening programme to be implemented and have high uptake, it is important to raise patient awareness of COPD risk factors and symptoms and provide training and additional resources for primary care. In particular, it is important to ensure that management pathways for diagnosed COPD patients are optimised before further cases are identified.

Strengths and limitations

To our knowledge, this was the first study to explore perceptions of patients and health-care providers on different stages of case-finding. However, we did not explore experiences of the approach to recruitment for screening (questionnaire at GP surgery or by post) and no participant commented on this. In addition, we did not invite and have not captured the views of people who reported no chronic respiratory symptoms as part of screening. Furthermore, inviting patients in the context of research may not reflect views on screening in practice. For health-care staff, those who participated are likely to be more engaged in case-finding and their views may represent those who are more proactive in management of case-found COPD.

Objective (iv): to describe the clinical management of screen-detected chronic obstructive pulmonary disease patients in primary care and compare management in those who were versus those who were not on the practice chronic obstructive pulmonary disease registers (work package 1iv, manuscript submitted)

Rationale

From a public health perspective, screening is more than a screening test. To have an impact on clinical outcomes, a number of criteria need to be fulfilled and, in the UK, the National Screening Committee considers these carefully before recommending commencement of a population screening programme.

The criteria relate to the condition, the screening test, the treatments available for those who are screen detected and the characteristics of the programme and its implementation. In relation to the programme implementation, it is important to ensure that resources are available and pathways are in place to manage screen-detected individuals. In the UK, NICE has set out a pathway for the diagnosis and management of people with COPD.³¹ As part of the TargetCOPD trial, patients with chronic respiratory symptoms who attended spirometry screening had their results fed back to their GP, with a note for them to follow NICE guidelines for further management. However, there are few studies that have examined how patients diagnosed with COPD are subsequently managed and whether or not primary care staff follow recommended pathways for managing these patients. We therefore obtained data from GP EHRs and self-reported data from case-found patients (those with airflow obstruction on spirometry who fulfil the NICE recommended criteria for diagnosing COPD) to describe the clinical management of case-found COPD patients (identified through the TargetCOPD trial) and compare this with that of patients newly diagnosed with COPD through routine care. In addition, we compared characteristics and management for those who were or were not entered on to the practice COPD register.

What we did

We identified patients who had been newly diagnosed with COPD (case-finding, $n = 857$; routinely diagnosed, $n = 764$) during the period August 2012 to June 2014 in the 54 GP practices that took part in the TargetCOPD trial. Data on demographic and clinical characteristics, as well as a range of clinical assessments and interventions recommended by NICE for people with COPD, were extracted from EHRs for a subset of patients covering the period April 2011 to September 2017. In addition, patients who had been identified through case-finding were invited to complete a health questionnaire around 5 years after their first diagnosis, in March 2018, with a reminder 2 months later.

For all patients, we determined whether or not they had been added to the practice COPD register used in reporting for the Quality and Outcomes Framework (QOF) by the end of the TargetCOPD trial period. The number of COPD-related clinical assessments and interventions were summed to form a clinical management score. Multilevel logistic regression was used to assess for associations between participant characteristics and the likelihood of being added to a disease register, comparing those who were identified through case-finding with those routinely diagnosed. Multilevel linear regression was used to assess associations between participant characteristics, COPD disease registration and the clinical management score.

What we found

Figure 2 shows a summary of participants included in these analyses. The primary analysis showed that just over one-fifth (182/857; 21.2%) of case-found patients, but almost all of the routinely diagnosed patients (708/764; 92.7%), had been added to the QOF COPD register within 12 months of assessment [median time from trial spirometry assessment to COPD registration 152 days, interquartile range (IQR) 72–258]. Factors associated with a higher likelihood of COPD registration among case-found patients were current and former smoking (adjusted OR 8.68, 95% CI 2.53 to 29.82, vs. OR 6.32, 95% CI 1.88 to 21.29, respectively) and lower percentage of predicted FEV₁ (OR 0.96, 95% CI 0.95 to 0.98).

Electronic health record data were available for 532 out of 1629 patients (identified through case-finding, $n = 344$; identified through usual care, $n = 188$) (Table 1). The characteristics of participants with and without EHR data were broadly similar. Factors associated with a higher clinical management score were being on the COPD register (adjusted β 5.06, 95% CI 4.36 to 5.75, which means that the score was on average 5 units higher for those on the COPD register than for those not on the register) and a higher number of comorbidities (adjusted β 0.38, 95% CI 0.11 to 0.65, which means that the score increased by 0.38 units for each additional comorbidity). Although of only borderline statistical significance, there was also a negative association with being case-found rather than routinely diagnosed (adjusted β -0.69, 95% CI -1.44 to 0.07).

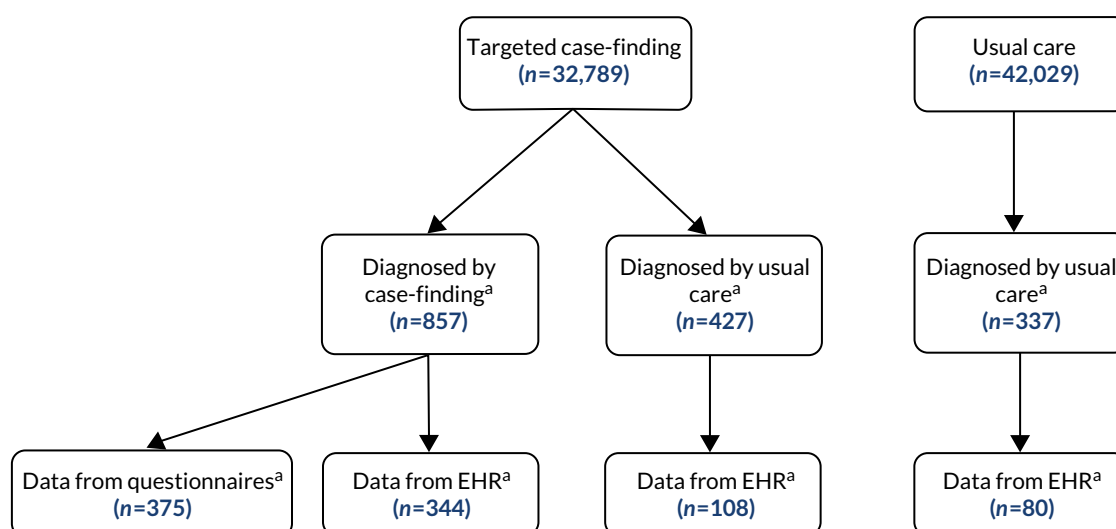


FIGURE 2 Flow of participants contributing to analyses for this study. a, Included in current study.

TABLE 1 Clinical management during the 2-year follow-up of participants with EHR data who were case-found vs. those clinically diagnosed through usual care

	Diagnosis			
	Case-finding (N = 344)		Usual care (N = 188)	
	n ^a	%	n ^a	%
Clinical assessment				
MRC dyspnoea score recorded	98	28.5	171	91.0
CAT score recorded	36	10.5	94	50.0
Spirometry undertaken	48	14.0	79	42.0
COPD severity recorded	33	9.6	96	51.1
BMI recorded	244	70.9	168	89.4
Oxygen saturations recorded	41	11.9	55	29.3
Chest X-ray undertaken	13	3.8	9	4.8
Depression screen undertaken	54	15.7	55	29.3
Clinical intervention				
Listed on COPD register	78	22.7	175	93.1
Care plan recorded	38	11.0	97	51.6
Annual review undertaken	91	26.5	170	90.4
Smoking cessation counselling provided	157	45.6	139	73.9
Nicotine replacement therapy	27	7.8	17	9.0
Influenza vaccination provided	240	69.8	138	73.4
Pneumococcal vaccine provided	19	5.6	23	12.2
Pulmonary rehabilitation provided	17	4.9	42	22.3
Inhaler technique assessed	56	16.3	116	61.7

TABLE 1 Clinical management during the 2-year follow-up of participants with EHR data who were case-found vs. those clinically diagnosed through usual care (continued)

	Diagnosis			
	Case-finding (N = 344)		Usual care (N = 188)	
	n ^a	%	n ^a	%
Inhaler prescribed				
Salbutamol	128	37.2	152	80.9
Ipratropium	5	1.5	10	5.3
Salmeterol	3	0.9	10	5.3
Fluticasone	3	0.9	1	0.5
Budesonide	0	0.0	0	0.0
Beclometasone	20	5.8	13	6.9
Fluticasone/salmeterol	33	9.7	70	37.2
Budesonide/formoterol	12	3.5	23	12.2
Any of the above inhalers	134	39.0	163	86.7
Antibiotic rescue pack				
Prednisolone	10	2.9	43	22.9
Prednisolone	51	14.8	96	51.1
Clinical management score				
< 5	225	65.4	17	9.0
5 to 9	83	24.1	73	38.8
≥ 10	33	9.6	98	52.1
Median (IQR)	3	2-5	10	7-12
BMI, body mass index; CAT, COPD Assessment Test; MRC, Medical Research Council. a Number of participants who received the clinical assessment or intervention.				

Self-reported questionnaire data were available for 375 out of 857 case-found patients. Only one-fifth of these patients were on the COPD register and, overall, one-third were aware of their diagnosis through their GP (88.5% of those on the COPD register vs. 17.5% of those not on the register). Around 45% had attended a COPD annual review, with the proportion being higher for those on the COPD register (83.3% vs. 34.7%). Factors associated with a higher clinical management score in this group were having a larger number of comorbidities (adjusted β 0.38, 95% CI 0.10 to 0.65), higher COPD Assessment Test (CAT) score (adjusted β 0.05, 95% CI 0.01 to 0.08) and lower percentage of predicted FEV₁ (adjusted β -0.03, 95% CI -0.04 to -0.01). Being on the COPD register was also significantly associated with a higher management score (adjusted β 3.48, 95% CI 2.81 to 4.15).

A proportionately high number of case-found patients with COPD were not added to practice COPD registers and these patients were less likely to receive recommended effective treatments for their condition. Overall, even those who were on the COPD register did not receive all recommended interventions, including smoking cessation advice or referral to pulmonary rehabilitation.

Strengths and limitations

This is one of the largest studies to evaluate the clinical management of screen-detected COPD patients in primary care. The lack of availability of EHR data on all trial participants was a limitation, and the validity of the EHR data is dependent on the clinical coding practices used. Nevertheless, the missing data are likely to be random, based on similarity of characteristics between those with and without data. Furthermore, the self-reported data from those who responded to questionnaires broadly verified the findings from health records.

Objective (v): to assess the long-term effectiveness of case-finding for chronic obstructive pulmonary disease on respiratory hospitalisations and mortality (work package 1v, manuscript in preparation) and objective (vi): to compare outcomes (including health-related quality of life) among screen-detected chronic obstructive pulmonary disease patients in primary care who were managed adequately by their general practitioner (based on the practice chronic obstructive pulmonary disease registers) with those who were not

Rationale

Since starting our programme of work, the UK National Screening Committee undertook a review to consider screening for COPD^{44,45} and the USPSTF updated their review.⁴⁶ Both recommended against screening for the time being, citing the need to establish evidence on clinical effectiveness of early identification before recommending systematic programmes for screening. The benefits of case-finding in improving health-related quality of life (HRQoL) and QALY gains has also not been previously studied.

Through our original trial, the infrastructure was in place to assess whether or not screening and early detection of COPD benefited patients in the longer term. We therefore sought a variation to the contract to extend follow-up and to link data on all patients who were part of the original trial with routinely available data. We obtained data on all eligible participants from NHS Digital on hospitalisations [through Hospital Episode Statistics (HES) data] and mortality, from the start of the trial until the last date available. We also sought approval from the National Research Ethics Committee and legal approval from the Confidentiality Advisory Group to obtain relevant patient identifiable data from GP practice records through an opt-out process and hold these temporarily to allow data linkage with the data obtained from NHS Digital. We were then able to compare outcomes among those who were in practices where active screening took place with those in the routine care arm practices (WP1v).

Additionally, to improve the input into the health economic model developed previously, we sought to obtain additional data on quality of life among screen-detected COPD patients some years after diagnosis and to compare outcomes among those who were managed in accordance with NICE guidelines with outcomes among those who were not.

What we did

Data on mortality and hospitalisations (all-cause and respiratory) were obtained for all eligible patients (who were alive at the start of the intervention, $n = 74,693$) from 54 participating practices in the TargetCOPD trial. Patient demographic data and information on whether or not the patient was on the practice QoF COPD register within 12 months of the trial were obtained from GP records. We also administered a questionnaire in 2017/18 to all case-found patients identified through the TargetCOPD trial to invite them to respond to questions on quality of life as well as their health and treatments received for COPD. Cox proportional hazard models, using random effects to account for clusters and adjusted for potential confounding factors, were used to model the time to event outcomes (death, first all-cause hospital admission and first respiratory hospital admission) in the intervention (active or targeted) and routine care arms. The time to event was censored at the death (for admission outcomes) or data extraction (30 September 2017 for hospital admissions and 13 October 2017 for deaths) if no event occurred. We also compared outcomes for the two intervention arms (active and opportunistic). Finally, for screen-detected cases, we compared mortality and hospitalisation as well as HRQoL measures [EuroQol-5 Dimensions (EQ-5D) and CAT scores] among those who were or were not added to the practice QoF register. Based on data from objective v, we used addition to the practice COPD register as a proxy measure for being better managed and treated for COPD. Analyses were adjusted for baseline values as well as for a range of potential confounders, including age, sex, ethnicity and baseline values for lung function, comorbidities and smoking status.

What we found

Among the 32,743 participants in the case-finding arms, 1557 had a respiratory hospitalisation compared with 1899 among the 41,950 participants in the routine arm over a mean follow-up period of 4.3 years [adjusted hazard ratio (HR) 1.04, 95% CI 0.73 to 1.47]. The corresponding HR for all-cause hospitalisation and mortality were 1.06 (95% CI 0.66 to 1.71) and 1.15 (95% CI 0.82 to 1.61), respectively, suggesting that, overall, there was no significant difference in risk of first hospitalisation and mortality between those who were in the screening arm compared with those in the routine care arm of the trial.

Within the two intervention groups in the case-finding arm there was no statistically significant difference between groups in terms of overall hospitalisations and mortality (adjusted HR 1.01, 95% CI 0.98 to 1.04, and adjusted HR 1.08, 95% CI 0.96 to 1.20, respectively). The adjusted HR for respiratory hospitalisation in the active group compared with the opportunistic group was 1.14 (95% CI 1.02 to 1.27), indicating an increased hazard of respiratory admissions in the former group (where yield from screening was higher).

Comparison of outcomes for screen-detected patients who were on the QOF COPD register with those who were not also showed no statistically significant difference in relation to all-cause hospitalisation (adjusted HR 0.86, 95% CI 0.66 to 1.11), respiratory hospitalisation (adjusted HR 0.95, 95% CI 0.52 to 1.73) and mortality (adjusted HR 1.06, 95% CI 0.53 to 2.12).

Thus, despite screening resulting in a higher yield of undiagnosed cases of COPD, there was no difference between those who were in practices with or without screening in terms of clinical outcomes at 4 years. The poor clinical management of COPD generally, and very low addition of case-found patients (particularly those with less severe disease) to the practice COPD register, may be an explanation for the findings. Given these results, we did not undertake a health economic analysis to examine cost per hospital admission avoided or cost per life-year saved.

In the adjusted analyses examining HRQoL, there was no statistically significant difference in EQ-5D scores between the two groups (adjusted mean difference -0.006 , 95% CI -0.048 to 0.036). The adjusted mean CAT score was statistically significantly and clinically higher in those who were on the COPD register than in those who were not (mean difference 2.317, 95% CI 0.481 to 4.153), indicating a greater impact of COPD on their life and poorer quality of life. This difference is likely to reflect the more severe disease and characteristics of those who are added to the COPD register compared with those who are not, rather than being a result of how they were managed.

Strengths and limitations

To our knowledge, this is the first trial to report clinical outcomes from a large trial of screening for undiagnosed COPD. The trial was not powered to detect clinical outcomes because that was not the primary aim, but, nevertheless, it has provided reasonable effect estimates. The poor clinical management of people with screen-detected COPD limits the ability of detecting any potential benefits and thus the interpretation of findings. The low proportion of screen-detected patients being entered on the COPD register may explain the observed lack of effectiveness of screening.

Additional outputs and published analyses related to work package 1

The main TargetCOPD trial paper was disseminated more widely at respiratory conferences internationally and won the following awards:

- Royal College of General Practitioners (RCGP) award for 'best paper of the year 2016' in Category 2 (CVD, Renal, Respiratory, Oral, ENT & Ophthalmology).
- European Respiratory Society (ERS) best abstract in primary care 2015.
- American Thoracic Society (ATS) best abstract Clinical Problems Assembly 2015.
- Society for Academic Primary Care nomination for best abstract 2015.

Additional related papers include the following.

Jordan et al.⁴⁷

This was the protocol for the TargetCOPD trial, outlining the rationale, methods and analysis plan.

Miller et al.⁴⁸

In this analysis we used data from the TargetCOPD trial and compared how the application of two different definitions of airflow obstruction would impact on the clinical characteristics of the population who would be labelled as having COPD. The definition used in the trial was based on the ratio of FEV₁/FVC < 0.7 [the fixed ratio (FR)], which is recommended by NICE. The second definition was based on using the lower limit of normal (LLN) that is increasingly being recommended. We found that, among 2607 people who attended for spirometry, around one-third had airflow obstruction using the FR definition compared with 20% using the LLN definition. There was overlap between the two groups. However, those identified by the FR and not the LLN definition were older, had better lung function and fewer respiratory symptoms, but had a higher rate of heart disease. Overall, we demonstrated that using the FR rather than LLN identifies a greater proportion of individuals with cardiac, rather than respiratory, clinical characteristics.

Haroon et al.⁴⁹

This analysis used data from the TargetCOPD trial to develop a validated algorithm and risk score to target case-finding on those at highest risk of undiagnosed COPD and thus improve the efficiency of any future case-finding process. Although other COPD risk scores have been developed, this was the first that was based on identifying case-found COPD (rather than incident clinical COPD diagnosed through routine care) and is therefore more useful in the context of case-finding in primary care.

Haroon et al.⁵⁰

In this analysis we used a case-control study design to match incident COPD cases from 340 GP practice registers (using the UK Clinical Practice Research Datalink) to two controls (based on age, sex and practice). Predictive risk factors for COPD were identified from practice records and used to develop a clinical risk score. The risk score was validated using a sample from a further 20 practices. The model, including smoking status, history of asthma and lower respiratory tract infections, and prescription of salbutamol in the previous 3 years, resulted in reasonable prediction (c-statistic 0.85, 95% CI 0.83 to 0.86).

Haroon et al.⁵¹

This systematic review (based on studies from 1997 to 2013) summarised the uptake and yield from different approaches to screening for undiagnosed COPD in primary care. Data from three RCTs, one non-randomised trial and 35 uncontrolled studies showed that all approaches result in identification of new undiagnosed cases. The review suggested that targeting higher-risk individuals (e.g. smokers) and using questionnaires or handheld flow meters prior to diagnostic screening was likely to increase yield. However, it also highlighted the need for well-conducted RCTs.

Haroon et al.⁵²

This review compared the diagnostic accuracy of different COPD screening tests in primary care. A total of 10 studies were identified from 1997 to 2013 and included use of screening questionnaires [mainly the COPD Diagnostic Questionnaire (CDQ)], handheld flow meters [e.g. the copd-6 (Vitalograph Ltd, Buckingham, UK)] or a combination. Handheld flow meters demonstrated higher test accuracy than questionnaires but the review highlighted the need for high-quality evaluation of comparative screening strategies.

Work package 2: the Birmingham primary care chronic obstructive pulmonary disease cohort

Objective (i): to recruit a cohort of 2000 new and existing chronic obstructive pulmonary disease patients from general practices in the West Midlands (work package 2, linked to work package 1, published)⁵³

Rationale

The natural history of COPD is still not understood, and several expert reviews have highlighted a need to further investigate both old and new longitudinal data.^{5,15} Prior to this programme, a number of relevant COPD disease cohorts had been established,⁵⁴⁻⁵⁶ but these included patients with more advanced disease from secondary care settings, with short duration of follow-up, and were mainly of small size. Other large population cohorts have also been used to address questions relevant to COPD.⁵⁷⁻⁶⁰ However, because these were not specifically set up to address COPD, not all relevant measures were undertaken and the quality of lung function was not always prioritised. There were no UK primary care COPD cohorts with patients representing the range of disease severity, particularly including people with mild/moderate disease, or a diverse socioeconomic mix. Furthermore, existing cohort studies included neither people with COPD who were identified through case-finding nor patients reporting respiratory symptoms but who had normal lung function [former Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 0].⁶¹ The evidence on progression to COPD in the latter group is limited and contradictory,⁶²⁻⁶⁴ and methods for assessing symptoms are inconsistent.^{62,65} The clinical relevance and natural history for this patient group and screen-detected cases are unclear.

What we did

We recruited 2305 patients aged ≥ 40 years from 71 practices across the West Midlands (*Figure 3*), comprising 1564 patients with previously diagnosed COPD, 330 previously undiagnosed patients with respiratory symptoms and airflow obstruction confirmed by spirometry (case-found COPD) and 411 symptomatic patients with normal lung function confirmed by spirometry.⁵³

Baseline assessments were undertaken by trained researchers using standardised protocols between 2012 and 2014 (*Figure 4*). Assessments included high-quality pre- and post-bronchodilator spirometry using an ndd EasyOne[®] spirometer (ndd Medizintechnik AG, Zurich, Switzerland). Other measurements included height and weight, body fat percentage estimation using the Tanita BC-420SMA Body Composition Analyser (Tanita Europe BV, Amsterdam, the Netherlands), assessment of grip strength using a Saehan Hydraulic Hand Dynamometer (Saehan Corp., Masan, Republic of Korea) and assessment of exercise capacity using the sit-to-stand test. In addition, trained researchers used face-to-face interviews to obtain occupational history. Information on skill content of occupations was used to assign a four-digit standard occupational classification (SOC2010)⁶⁶ code for current or main occupation using the CASCOT (computer assisted structured coding tool) software (online version, Office for National Statistics, Newport, UK).

Participants were also asked to complete questionnaires that sought data on demographic characteristics, lifestyle (smoking history and exercise habits), symptoms, exacerbation history, general health, diagnosed medical conditions, health-care usage and the home environment (see *Appendix 3*). HRQoL was assessed using disease-specific (CAT)⁶⁷ and generic (EQ5D)⁶⁸ instruments, and the Patient Health Questionnaire-9 (PHQ-9)⁶⁹ instrument was used to screen for depression. Work productivity was assessed through questions on work absence and presenteeism using the Stanford Presenteeism Scale (SPS-6)⁷⁰ and the Work Productivity and Activity Impairment questionnaire (WPAI).⁷¹

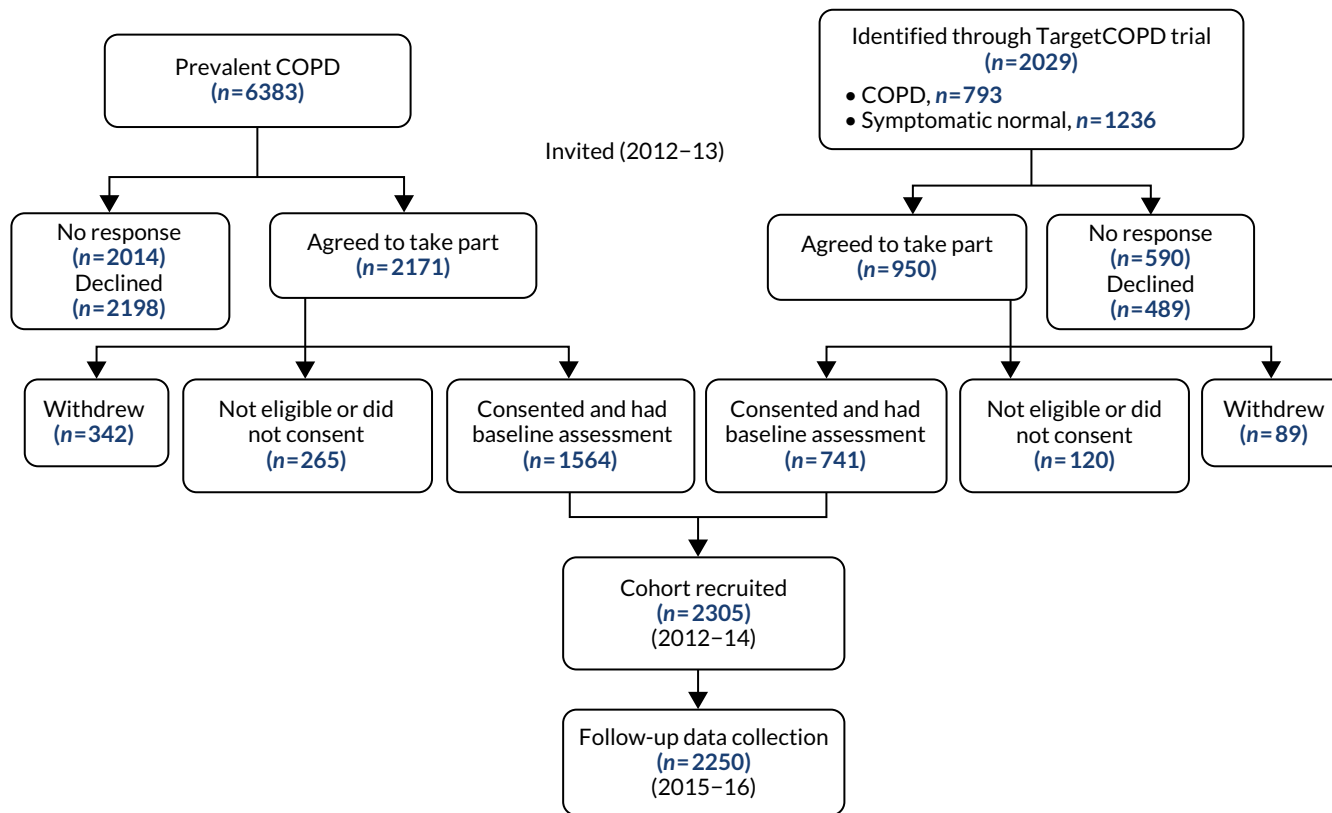


FIGURE 3 Flow chart of patient recruitment and assessment for the Birmingham COPD cohort study.

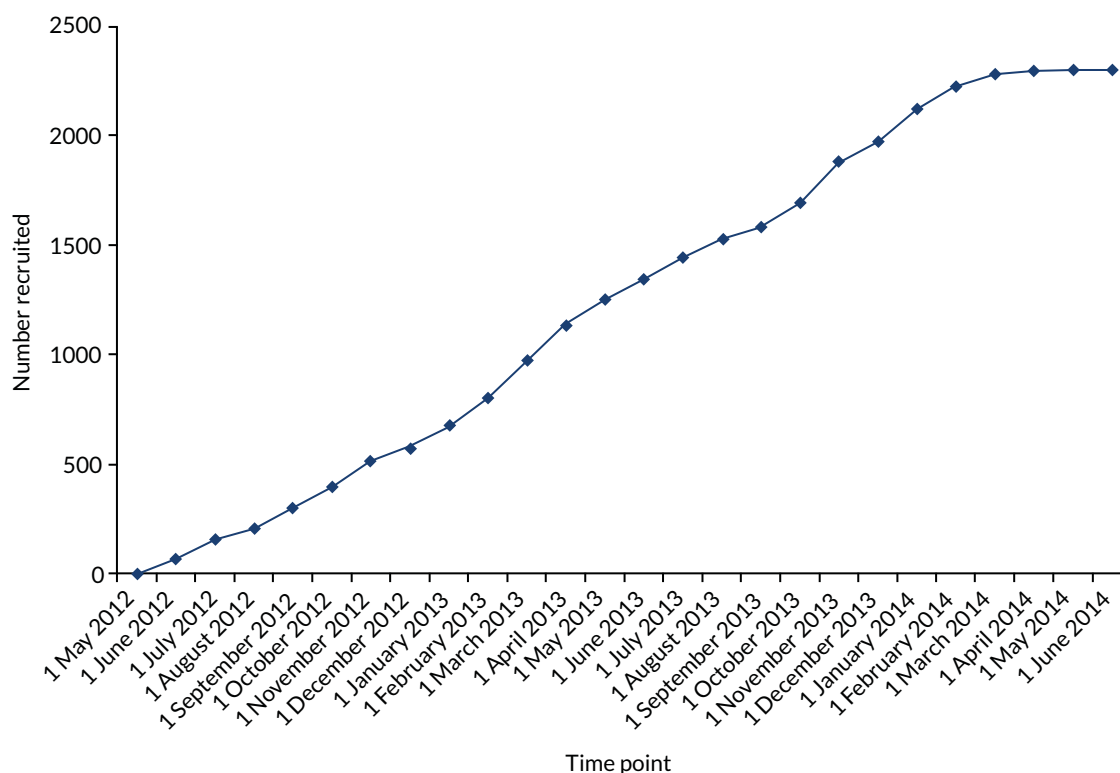


FIGURE 4 Cumulative number of cohort participants recruited and having baseline assessments by month.

At 6-monthly intervals, patients were sent follow-up questionnaires by post. All follow-up questionnaires included items on employment, general health, lung health, exacerbations, new diagnoses, attendance at pulmonary rehabilitation, health-care utilisation, smoking history, medications, depression and HRQoL. Some questionnaires included additional items, which are summarised in *Table 2*.

Patients were invited for a final assessment visit around 3 years after baseline (2015–16). In addition to post-bronchodilator spirometry, other baseline assessment measures and questionnaires were repeated. Cohort participants' routine data on comorbidities and medications were extracted from GP records. Linked data on hospital episodes and mortality were also obtained from NHS Digital for the period 1 April 2012 to 31 March 2016.

TABLE 2 Cohort questionnaire items and response rate at different follow-up points

Questionnaire	Special items in questionnaire	Response rate (%)
6 months	Self-management, exercise, COPD knowledge, major events	73.0
12 months	Major events	67.6
18 months	Handwashing, diet	69.2
24 months	Self-management, handwashing, exercise, self-efficacy	66.1
30 months	Pain symptoms, fatigue	62.8
Follow-up assessment	Exercise, smoking cessation, e-cigarette use, major events, sleep, vitamin use	88.3
Supplementary	Anxiety, illness perception, self-perception	78.8

Establishment of this cohort allowed important questions of relevance to patient benefit to be addressed (WP2i).

What we found

Follow-up data were available for 2250 patients (97.6%), and almost two-thirds (1469, 63.7%) returned for face-to-face follow-up assessment. Six-monthly questionnaires were completed by around two-thirds of patients (62.8–73.0%; see *Table 2*). In the initial 2 years of follow-up, 267 (12%) patients had at least one respiratory-related hospital admission, based on HES data. Over the entire period of follow-up (minimum 1.8 years, maximum 3.8 years), 382 patients (17%) had at least one respiratory hospital admission and 170 (7%) had died at the time data were obtained from NHS Digital.

Strengths and limitations

We established one of the largest primary care COPD cohorts, which is novel in that it includes case-found patients. A limitation was that fewer than one-third of case-found patients agreed to join the cohort. Our recruitment strategy resulted in an over-representation of patients with less severe disease because patients had to be ambulatory. Despite attempts to include patients from diverse ethnic backgrounds, the majority were white.

Objective (ii): to test the validity of existing chronic obstructive pulmonary disease prognostic models in a primary care chronic obstructive pulmonary disease population (work package 2, published);⁷² and objective (iii): to develop a prognostic model (BLISS index) to predict respiratory hospitalisations suitable for a primary care population (work package 2, drafted, see *Appendix 4*)

Rationale

A better understanding of factors predicting prognosis and the development of a prognostic model can facilitate doctor–patient consultations and inform management decisions and health service planning. For COPD, a simple measure of lung function, FEV₁, has historically been used to grade severity. However, there is increasing recognition that this measure is not a good predictor of clinical outcomes. Alternative measures of lung function may improve diagnostic⁷³ and prognostic ability.^{74,75}

A number of studies have also described a range of factors other than lung function that are associated with COPD progression, deriving prognostic indices. The first [BODE (body mass index, airflow obstruction, dyspnoea, and exercise) index] was developed to predict mortality risk in those with COPD.⁵⁶ However, the method of development was not clear, its validity has not always been confirmed and not all measures are practical in non-specialist settings.⁷⁶ Since then, several other prognostic models have been developed and, since we started the programme, a number of systematic reviews have been undertaken to summarise these.^{77–79} The reviews show that existing prognostic models are heterogeneous in terms of the number and type of predictors, the prognostic outcome, time horizon and statistical approach. Most focus on predicting mortality risk,^{56,76,80–82} although others were developed to predict additional outcomes such as exacerbations,^{83,84} COPD-related hospitalisation,⁸⁵ respiratory hospital attendance/admission⁸⁶ and exacerbation or hospitalisation.^{87,88} Only three indices^{84,87,88} were derived from primary care populations, despite this being where most COPD patients are managed, and most included patients with more severe established disease. No models were developed in populations that included case-found patients. Few studies were validated or used recommended statistical approaches for deriving the model.

The most recent review showed that the ADO index was most discriminatory in predicting mortality.⁷⁸ For a prognostic model to be used by clinicians, it needs to be simple and capture the required patient data with minimum resource;⁸⁹ the ADO index fulfils these criteria. We therefore undertook validation of the ADO index for mortality within our cohort (WP2, objective ii).

However, in relation to predicting respiratory hospitalisation, which is an important outcome to consider, current models have moderate discriminative ability. This suggests that other relevant predictors are missing from these prognostic models. We therefore derived a new COPD prognostic model, the BLISS index, for use in a primary care population (with 2-year respiratory hospitalisation as primary outcome and all-cause hospitalisation, exacerbations, primary care consultations and mortality as secondary outcomes), using recommended statistical techniques (WP2, objective iii, draft paper; see *Appendix 4*).

What we did (objective ii)

We validated the ADO index using data from 1701 patients from the Birmingham COPD cohort study (case-found or on the practice COPD register) who had complete data for the variables required for this study. We externally validated the ADO index for predicting 3-year mortality, with 1- and 2-year mortality as secondary end points. Discrimination was calculated using area under the curve (AUC), also known as the *c*-statistic, and calibration was assessed using a calibration plot with locally weighted scatterplot smoothing (LOWESS) and measures such as the calibration slope. In sensitivity analyses, we included only patients with existing COPD and those with complete data.

What we found (objective ii)

The ADO index was discriminatory for predicting 3-year mortality (*c*-statistic 0.74, 95% CI 0.69 to 0.79), with similar discriminatory ability for 1- and 2-year mortality (*c*-statistic 0.73, 95% CI 0.66 to 0.80, and *c*-statistic 0.72, 95% CI 0.67 to 0.76, respectively). The ADO index overpredicted mortality at each time point, which was more pronounced at 1- and 2-year mortality time points (calibration slopes 0.95, 0.79 and 0.79 for 3-, 2- and 1-year mortality, respectively) and in those with higher baseline ADO scores. Thus, although the ADO index shows promising discrimination in a primary care population, the model may need to be recalibrated if the ADO index is used to provide well-calibrated risk predictions for 1- or 2-year mortality. Discrimination and calibration were similar in sensitivity analyses.

What we did (objective iii)

To develop and internally validate a new prognostic model in primary care to predict respiratory hospital admissions within 2 years, we linked self-reported and clinical data for all patients with COPD from the Birmingham COPD cohort (331 case-found and 1558 previously diagnosed) with routine HES obtained through NHS Digital. The primary outcome for the prognostic model was the occurrence of a respiratory-related hospital admission (using primary diagnostic codes) from entry to the cohort study up to 2 years (May 2012 to June 2014). Secondary analysis considered outcomes during the full period until the NHS Digital data were obtained (1 April 2016). The maximum follow-up time was around 4 years.

A list of 23 candidate variables was drawn up based on those included in other models for COPD, along with other variables identified by a consensus panel comprising study investigators, clinicians and patients. The degree of airflow obstruction was deemed clinically important but, owing to the documented statistical problems with the commonly used FEV₁% predicted (FEV₁ as a percentage of what would be predicted as normal),⁷⁵ the best variable to be included in the model was not clear. We therefore tested three variables as candidate predictors in the model [FEV₁% predicted, forced expiratory volume in 1 second quotient (FEV₁Q), and FEV₁/height²]. With 267 events for the primary outcome, up to 26 candidate variables could be used, based on the rule of thumb of 10 events per candidate variable.⁹⁰

The model was developed using backward elimination with $p < 0.157$ for retention. Fractional polynomials were considered and multiple imputation using chained equations was used for missing data. Discrimination was assessed using the *c*-statistic and calibration was also assessed. Bootstrapping was used for internal validation and the optimum-adjusted performance statistics were presented. A sensitivity analysis was conducted using only those with previously diagnosed COPD.

What we found (objective iii)

Over a median follow-up of 2.9 years (range 1.8 to 3.8 years), 382 participants (16%) had a respiratory admission and 267 (12%) had a respiratory admission in the primary 2-year period. Participants with hospitalisations were more likely to be older (70.3 vs. 67.0 years; $p < 0.001$), be male (66% vs. 59%; $p = 0.017$), be more deprived [median Index of Multiple Deprivation (IMD) score of 30.3 vs. 24.4; $p = 0.0025$], have a lower body mass index (BMI) (mean 28.2 vs. 28.8 kg/m²; $p = 0.108$), have more severe airflow obstruction (mean FEV₁% predicted 56.5% vs. 75.2%), have worse dyspnoea [Medical Research Council (MRC) dyspnoea grade 3 57.5% vs. 51%; $p < 0.001$] and have worse quality-of-life scores (median CAT score 24 vs. 17; $p < 0.001$). They were more likely to report previous exacerbations based on the use of antibiotics or steroids (60% vs. 43%; $p < 0.001$) and to report previous hospitalisations in the previous 12 months (18.4% vs. 2.6%; $p < 0.001$). Participants with hospitalisations were also more likely to report a higher rate of vapours, gases, dusts or fumes (VGDF) (71% vs. 62%; $p = 0.004$), to report exposure to smoking (31% vs. 27% current smokers; $p = 0.019$) and to have diabetes (24% vs. 15%; $p = 0.001$) and cardiovascular disease (20% vs. 15% with coronary heart disease; $p = 0.049$).

Using a pragmatic approach to model development, and including only variables that are widely available or feasible to obtain in primary care, six variables were retained in the final developed model: age, CAT score, respiratory admissions in the previous 12 months, BMI, diabetes and FEV₁% predicted. After adjustment for optimism, the primary model performed well in discriminating between those who will and those who will not have 2-year respiratory admissions (*c*-statistic 0.75, 95% CI 0.72 to 0.79). Four further variables were included in the secondary analysis but had similar score performance. Sensitivity analysis with prevalent COPD cases resulted in an identical apparent *c*-statistic but included smoking status in addition to the six variables in the primary model. Overall, the BLISS score may perform better in predicting respiratory admissions than the scores currently available, but further research is required to compare this model with existing ones in other data sets. Important next steps are external validation, proposing and evaluating a model of use to guide patient management, and exploration of the best ways to implement such a score in primary care practice.

Strengths and limitations

We used recommended and up-to-date approaches for our validation study and model development, overcoming limitations of previous studies. Using data from a research cohort (the Birmingham primary care COPD cohort) meant that measurements were of high quality and undertaken at prescribed time points. However, the cohort population may not be fully generalisable to primary care because patients with more severe disease who were housebound were excluded. Including screen-detected patients was a strength and limitation but sensitivity analyses excluding these patients did not substantially alter the findings. For model development, although the variable components for the score are relatively simple, these may not be routinely collected or available, and calculation of the score requires software.

Objective (iv): to explore barriers to and enablers of participation in physical activity among people with chronic obstructive pulmonary disease in primary care (work package 2, published)⁹¹**Rationale**

Although the majority of people with COPD who are likely to be detected through case-finding could be offered evidence-based interventions, there are few effective interventions for those with milder disease. One intervention that has received increasing interest is exercise. Observational studies have reported an association between higher PA levels and lower morbidity⁹²⁻⁹⁴ across the full range of COPD severity. Exercise is the cornerstone of pulmonary rehabilitation programmes (PRPs), which have been shown to have a positive impact on COPD symptoms and prognosis.⁹⁵ However, PRP provision is limited and uptake is low.⁹⁶ To better understand the motivation for PA engagement among people with COPD in the community, we explored perceived barriers and facilitators among people with COPD using the framework from social cognitive theory.

What we did

A purposive sample of 26 patients (age range 50–89 years; men, $n = 15$) from the Birmingham COPD cohort study, with a range of COPD severity, was recruited to participate in one of four focus groups. Thematic analysis was undertaken to identify key concepts related to their self-efficacy beliefs.

What we found

Several barriers to and enablers of PA closely related to self-efficacy beliefs and symptom severity were identified. The main barriers were health-related (fatigue, mobility problems, breathing issues caused by the weather), psychological (embarrassment, fear, frustration/disappointment), attitudinal (lack of feeling in control of their condition, disregard of PA benefits, older age perception) and motivational. The main enabling factors were related to motivation (PA as part of caring duties, deriving enjoyment from activity or the social aspects), attitudes (positive view of PA), self-regulation (e.g. keeping to a routine) and performance accomplishments (sense of achievement in fulfilling personal goals). This information can help to tailor management of people with COPD.

Strengths and limitations

The use of social cognitive theory in this study was novel, and allowed the identification of personal barriers related to perceptions, motivation and attitudes towards physical activity, which went beyond the external barriers identified in previous studies. This understanding can inform interventions that have the potential to improve attendance and adherence. Furthermore, by including distinct subgroups of patients, we identified context-specific factors, such as barriers specific to those who are in paid employment, thereby informing the tailoring of future interventions.

However, the study participants predominantly had mild to moderate COPD and so the findings may not reflect the views of those with more severe disease. Furthermore, the voluntary nature of participation may have meant that the views of some who were less interested in PA were not included. The emergence of themes may also have been influenced by the use of social cognitive theory, and potentially different themes might have dominated had a different theoretical framework been used.

Other collaborations and analyses of cohort data

One of the aims of establishing a cohort was to allow it to become a platform for testing other hypotheses and interventions. As a result, several groups, including postgraduate students and other collaborators, worked with us to introduce discrete questions in some of the follow-up questionnaires or undertook analyses from the data collected for the cohort study. The main substudies are described below.

Cohort data used for analyses leading to a PhD thesis: Buni⁹⁷

Rationale

There has long been uncertainty about the nature and prognosis of people with chronic respiratory symptoms who do not yet meet the accepted airflow obstruction criteria for COPD.⁹⁸ In 2001, the GOLD committee included an additional 'at-risk' stage in the description of COPD patients with a view to considering early interventions. Patients in this stage (known as GOLD stage 0) were thought to be 'at risk' of developing COPD in the future.⁶¹ However, in 2006, GOLD stage 0 was removed from the classification owing to a lack of supporting evidence regarding progression to diagnosed COPD. Nevertheless, there remain many patients (particularly smokers) in the population with such symptoms; some patients even carry a formal diagnosis of COPD and are therefore potentially 'overdiagnosed'. It is debated whether these patients represent a group with 'pre-clinical' COPD or if they have other conditions that explain their symptoms. We undertook a range of primary and secondary data analyses to help answer these questions.

What we did

We undertook three linked systematic reviews to identify and assess published studies that (1) examined the risk of developing COPD among GOLD stage 0 patients compared with the normal population, (2) examined the prognosis of GOLD 0 patients compared with established COPD patients and/or (3) evaluated factors that affected the prognosis of GOLD 0 patients. The primary studies included analysis of (a) data from the 2010 Health Survey for England (HSE)⁹⁹ to evaluate the independent effect of respiratory symptoms by airflow obstruction on quality of life, (b) cross-sectional data from the Birmingham COPD cohort study to compare the characteristics and health outcomes of GOLD 0 patients with newly diagnosed (case-found) COPD patients who had airflow obstruction and (c) cross-sectional data from the Birmingham COPD cohort study to compare the characteristics and health outcomes of people on the GP COPD register who did not have airflow obstruction (overdiagnosed) with those of people who had spirometric obstruction.

What we found

The systematic reviews revealed very few published studies evaluating the prognosis of people with GOLD 0 symptoms, and the studies that were found were heterogeneous in design, populations and outcomes. A tentative conclusion was that those with GOLD 0 symptoms may show faster decline in FEV₁ than the normal population, but the risk of developing COPD was not consistent. Persistent GOLD 0 symptoms may be an important predictor of development of COPD and FEV₁ decline. Persistent symptoms were associated with continued smoking and, in some studies, the presence of metabolic syndrome. GOLD 0 patients had similar risks of mortality to GOLD 1 patients, and those who were current smokers had similar risks to GOLD 2 patients. GOLD 0 patients often had similar health-care use to established COPD patients.

The HSE analyses revealed a gradient of effect on quality of life from 'normal' to those with COPD. Asymptomatic patients with airflow obstruction only were much more similar to 'normals', and those with GOLD 0 were more similar to those with both symptoms and airflow obstruction (i.e. defined as COPD). Dyspnoea and wheeze were more strongly associated with poor quality of life than chronic productive cough.

Analyses of the Birmingham COPD cohort showed that GOLD 0 patients had similar consumption of health-care resources to those newly identified with COPD, additionally indicating similar quality of life, exercise capacity and exacerbation-like events in these two groups. GOLD 0 patients were more likely to be female, to be obese and to have multiple comorbidities (e.g. cardiovascular disease, hypertension, diabetes and depression) than diagnosed COPD patients, but they were not more likely to have either diagnosed or undiagnosed asthma (assessed using GOLD/ATS definition of bronchodilator reversibility; a change of > 12% of baseline FEV₁ if this exceeds 200 ml). Overall, 10% had reversible airflow obstruction suggestive of asthma.

Overdiagnosed COPD patients (≈14% on UK COPD registers) were also more likely to be female, to have never smoked and to be obese (19% had restrictive pattern disease) and were slightly more likely to have multiple comorbidities. Around 20% of these patients had spirometric abnormalities consistent with restrictive lung disease. Their quality of life, exacerbation history, exercise capacity and health-care utilisation were very similar to those of GOLD 0 patients.

In conclusion, the presence of respiratory symptoms is epidemiologically and clinically relevant. GOLD 0 patients have similar poor quality of life and health-care consumption to those with mild COPD. It is still uncertain whether this group will develop COPD or if they are ill because they have other conditions. It is also possible that spirometric criteria for defining COPD need to be reconsidered. Future longitudinal studies are needed to further investigate GOLD stage 0 and to inform management guidelines that may include earlier interventions. This is important to help improve patients' quality of life, reduce the risk of misdiagnosis and reduce inappropriate health-care resource use.

Collaboration with Professor Mike Thomas from the University of Southampton: Brien et al.¹⁰⁰

This analysis explored demographic factors, lung function/COPD-related symptoms and psychosocial/behavioural factors associated with quality-of-life impairment (using COPD CAT scores) in people with COPD. In a multivariable model, we showed that dyspnoea, illness perception, dysfunctional breathing symptoms and depression explained most of the impairment in quality of life. Thus, interventions targeting psychological factors could improve outcomes in people with COPD.

Linked trial funded through the NIHR National School of Primary Care Research: Jolly et al.¹⁰¹

This trial was a modification of a WP in the original programme grant, with additional funding. Overall, 577 people with earlier-stage COPD (MRC dyspnoea grade 1 or 2) were recruited from general practices (2014–15). Participants were randomised to a nurse-delivered telephone health coaching intervention (smoking cessation, increasing PA, medication management and action-planning) or usual care. Compared with usual care, participants in the intervention group reported significantly greater PA at 6 months.

Dickens et al.¹⁰²

We obtained additional funding from the National Institute for Health Research (NIHR) School of Primary Care Research to undertake a linked study to assess the accuracy of microspirometry as a screening tool for undiagnosed COPD. The relevant measurements were undertaken during cohort participants' visits. We compared lung function measures obtained from the Vitalograph® (Vitalograph Ltd, Buckingham, UK) lung monitor with post-bronchodilator confirmatory spirometry. We found that the optimal cut-off point for the lung monitor was a FEV_1/FEV_6 of < 0.78 , resulting in sensitivity of 82.8% (95% CI 78.3% to 86.7%) and specificity of 85.0% (95% CI 79.4% to 89.6%).

Cohort data used by Master of Public Health students: Khan et al.¹⁰³

In this analysis, the extent of self-management behaviour and support reported by cohort participants was described. The majority of 1078 responders reported taking medications as instructed and receiving annual influenza vaccinations. However, only 40% had self-management plans and half reported never having received advice on diet/exercise. Fewer than half of current smokers had been offered help to quit in the previous year. Having a self-management plan was associated with better medication adherence and better disease knowledge.

Cohort data used as part of a PhD thesis: Kostel¹⁰⁴

One chapter is dedicated to the focus groups exploring the views of COPD patients on PA.

Work package 3: chronic obstructive pulmonary disease and occupational performance

Objective (i): to examine factors associated with employment (published), absenteeism and presenteeism (published) among COPD patients of working age (work package 3)^{105,106}

Rationale

Among those with COPD in the UK, approximately 40% are below retirement age; of these, 25% are not able to work.¹⁰⁷ Among those who continue to work, COPD is likely to affect work capability through sickness absence (9% of all certified absences) and working while unwell (presenteeism).¹⁰⁸ Data from other countries suggest that people with COPD (including undiagnosed¹⁰⁹ and mild disease¹¹⁰) have a poorer employment history and retire earlier than people with normal lung function,¹¹¹ but there were no data quantifying this in the UK, and no studies to examine presenteeism or productivity among working adults with COPD. Indirect societal costs attributable to COPD (largely owing to absenteeism) are high. Studies based on other conditions suggest that presenteeism costs may exceed those associated with absenteeism.¹¹² Few studies have examined which factors among people with COPD are associated with lower employment and work productivity. This information could inform future interventions, which could, in turn, improve patients' work experience, thereby reducing the burden and societal costs related to COPD.

What we did

We undertook cross-sectional analysis of baseline data of patients from the Birmingham COPD cohort who were of working age. We compared the characteristics of those who were in paid employment with those who were not. Logistic regression analysis was used to assess the effects of sociodemographic, clinical and occupational characteristics on the likelihood of being employed. Using the subsample in paid employment, we examined characteristics associated with absenteeism (defined by self-report over the previous 12 months) and presenteeism (assessed using the Stanford Presenteeism Scale).

What we found

Among the 1889 people in the cohort who had COPD, 608 were of working age, of whom 248 (40.8%) were in work. Older age (60–64 years vs. 30–49 years: OR 0.28, 95% CI 0.12 to 0.65), lower educational level (no formal qualification vs. degree/higher level: OR 0.43, 95% CI 0.19 to 0.97), poorer prognostic score [highest vs. lowest quartile of modified BODE score: OR 0.10, 95% CI 0.03 to 0.33] and history of high occupational exposure to VGDF (high VGDF vs. no VGDF exposure: OR 0.32, 95% CI 0.12 to 0.85) were associated with a lower probability of being employed. Only the degree of breathlessness component within the BODE score was significantly associated with employment. Among those who were in paid employment, degree of breathlessness was the only factor associated with both absenteeism (high absenteeism in severe vs. mild dyspnoea: OR 1.84, 95% CI 0.54 to 6.27; $p < 0.01$) and presenteeism (working while unwell in severe vs. mild dyspnoea: OR 18.11, 95% CI 2.93 to 112.21; $p < 0.01$). Additionally, increasing history of occupational exposure to VGDF was independently associated with presenteeism (poor presenteeism in medium/high exposure vs. no exposure: OR 4.34, 95% CI 1.26 to 14.93; $p < 0.01$).

Based on these findings, future interventions should focus on managing breathlessness and reducing occupational exposures to VGDF to improve work capability among those with COPD.

Strengths and limitations

The inclusion of a wide range of patients with COPD from primary care, including case-found patients, was novel. The assessment of occupation in detail and linking with a job exposure matrix to estimate VGDF exposure was a strength. However, overall, the sample of participants in paid employment was small and the wide CIs for several estimates suggest that there was insufficient power to clarify associations. We did not have objective measures of absenteeism and some other measures were also based on self-report, which may introduce errors.

Objective (ii): to examine how disease progression (lung function decline, exacerbation) over time is associated with occupational performance (employment, absenteeism and presenteeism) among chronic obstructive pulmonary disease patients in employment (work package 3, manuscript in preparation)

Rationale

The burden of COPD on the working population is high. The relationship between sickness and disability and unemployment is poorly understood and could be better informed by longitudinal follow-up. A number of factors, including sociodemographic characteristics, the general economic environment and the severity of chronic disease, have an impact on employment and an individual's ability to work. We undertook longitudinal analysis to examine how disease progression is associated with occupational outcomes, adjusting for clinical, sociodemographic, occupational and labour market factors.

What we did

We used data collected during the follow-up period for those with COPD in the Birmingham COPD cohort study. Participants completed a series of questionnaires at baseline, providing information on their demographics, socioeconomic circumstances, health, lifestyle and occupation. At 6-monthly intervals they completed further questionnaires, reporting on changes in employment and, for those in paid employment, completed questions on presenteeism and absenteeism. Trained research assistants collected clinical information at two face-to-face assessments (baseline and the final follow-up), which included spirometry. We undertook longitudinal analyses, including participants who were in paid employment at baseline.

Four markers of disease progression were assessed: FEV₁ (no or limited decline vs. greater decline), number of respiratory-related hospital admissions, breathlessness (no increase vs. increase in MRC score) and symptom impact (no increase vs. increase in CAT score).

For the primary analyses, decline in FEV₁ was based on the following thresholds (comparing baseline spirometry values with those at the final follow-up): > 113.3 ml per year in men and > 90.1 ml per year in women. These were based on the upper limit of normal decline rates in FEV₁ described in healthy adults.¹¹³ Respiratory-related hospital admissions was calculated as the number of admissions during the study follow-up (continuous data). The minimal clinically important difference (MCID) for the MRC respiratory questionnaire (1-point increase)¹¹⁴ was used to define worsening breathlessness, where MRC scores were compared at two time points (baseline and final follow-up for each outcome measure). Additionally, the MCID value for the CAT score was used to define worsening symptom impact. However, because this varies in the current literature,¹¹⁵ two analyses were conducted. The primary analysis was based on an increase of < 2 or ≥ 2 points at the final follow-up.

Multivariable regression analyses were conducted to examine the effects of disease progression on each of the outcomes, adjusting for age, sex, educational attainment, social deprivation (using the IMD derived from participant home postcode), MRC score, GOLD staging, occupational exposure to VGDF in current job at baseline visit (paid employment and presenteeism analyses) and number of hours worked at baseline (absenteeism analysis).

What we found

Among the 248 participants with COPD who were in paid employment at baseline, follow-up data were available for 174 (70.2%). Among those who were followed up, 144 (82.8%) remained in paid employment and 30 (17.2%) who had initially been in paid employment became unemployed. The mean length of follow-up was 25.8 months [standard deviation (SD) 5.8 months].

Our point estimates were suggestive of an association between increasing number of respiratory-related hospital admissions (OR 0.32, 95% CI 0.09 to 1.14; $p = 0.08$), decline in FEV₁ (OR 0.64, 95% CI 0.11 to 3.71; $p = 0.62$) and worsening MRC dyspnoea score (OR 0.62, 95% CI 0.19 to 2.06; $p = 0.44$) and reduced probability of remaining in paid employment, but CIs were very wide and no firm conclusions were possible. We found no associations between worsening symptom impact (CAT score) and reduced probability of remaining in paid employment.

Prospective absenteeism data were available for 113 (59.8%) participants, with a mean length of follow-up of 19.5 months (SD 5.3 months). Among this group, 63 (55.8%) reported taking > 1 day off over the follow-up period. Absenteeism ranged from 0.5 to 180.0 days per year [mean 16.3 days off per year (SD 28.9 days off per year); median 6.0 days off per year (IQR 2.7–5.5 days off per year)]. In the total cohort population, the mean and median days off per year were 9.0 (SD 23.0) and 1.5 (IQR 0.0–7.0), respectively.

Worsening breathlessness [incidence rate ratio (IRR) 3.06, 95% CI 1.29 to 7.26; $p = 0.01$] and respiratory hospital admissions (IRR 2.01, 95% CI 1.09 to 3.69; $p = 0.03$) were associated with an increased risk of sickness absence duration, and point estimates suggested that worsening symptom impact (CAT score) might also have an effect, although CIs were wide. Associations between FEV₁ decline and sickness absence duration were not observed.

Follow-up data on presenteeism were available for 163 (86.2%) participants, among whom 43 (26.4%) had worsening presenteeism. Worsening presenteeism was significantly associated with worsening CAT score (OR 5.74, 95% CI 1.18 to 27.83; $p = 0.03$) and may be associated with worsening MRC dyspnoea score (OR 2.25, 95% CI 0.76 to 6.68; $p = 0.14$). No strong evidence of any patterns were observed between FEV₁ decline or respiratory-related admissions and worsening presenteeism.

In summary, disease progression, characterised by a greater number of respiratory hospital admissions (proxy for severe exacerbations) and worsening symptoms, may be associated with poorer work productivity. We did not find any associations between physiological decline, measured by increase in airflow obstruction, and occupational outcomes. Given the wide CIs, further research is needed to increase power to detect genuine associations.

Strengths and limitations

Although participants were drawn from a population with a wide range of sociodemographic, clinical and occupational characteristics, the analyses were based on a small sample size, resulting in low power and lack of precision for many estimates. The observed associations raise hypotheses for future research and have to be interpreted with caution. The length of follow-up (2.5 years on average) may be insufficient for observing a decline in lung function, and cut-off points for abnormal decline are not agreed. The study included an older working population and, therefore, a healthy worker survivor effect might apply.

Objective (iii): to assess the feasibility and benefits of offering formal occupational health assessment and subsequent recommendations aimed at improving work-based indices to people with chronic obstructive pulmonary disease in employment (work package 3, published PhD thesis)¹¹⁶

Rationale

A UK government report focused on the need to support individuals of working age to remain in or to return to employment from sickness absence.¹¹⁷ The report made a number of recommendations,

including the need for early workplace interventions, improved access to OH services and changes in sickness certification from 'sick' to 'fit' notes.¹¹⁸ The feasibility and effectiveness of early workplace interventions to support people with COPD with poor work performance has not been assessed.

What we did

Within the Birmingham COPD cohort, we invited all those who were in paid employment at baseline to a tailored assessment with an OH practitioner to explore and identify workplace factors that might negatively affect their work performance or exacerbate their condition, and to recommend appropriate modifications. Participants' self-management practices were also assessed. Recommendations were sent to the participant and, with their permission, to their GP and their employer. We examined acceptability (uptake of intervention and recommendations and exploration of participant views) and feasibility (proportion with recommendations and uptake) of the intervention.

What we found

Only 35 (11.3%) eligible patients agreed to take part; 109 (35.3%) declined and 153 (49.5%) did not respond. The main reasons for declining to take part included perceived lack of need ($n = 54$; 49.5%), had already made workplace adjustments ($n = 8$; 7.3%) and concern about employer involvement ($n = 5$; 4.6%). Most of those who took part ($n = 28$; 80.0%) required at least one OH recommendation and all required and received self-management recommendations. The most common OH recommendations were to modify working practices and to seek advice from the workplace OH department (or GP for those with limited access to OH services) about their respiratory symptoms in the work environment. However, only 28 out of 75 (37.3%) recommendations were reported as implementable by the interviewed participants.

Overall, the very low uptake rates for the intervention and low implementation of recommendations suggest that, in its current format, this is not a worthwhile intervention. In particular, participants were hesitant about employer involvement. Nevertheless, the finding that modifiable workplace adaptations and self-management actions were identified for almost all participants suggests that there may be benefit from such assessments to be undertaken in a different context.

Strengths and limitations

Although this was a novel intervention, the main limitation was the small sample size. Therefore, any patterns assessed among those who received recommendations should be interpreted with caution. Although the absence of randomisation and a control group makes it difficult to draw conclusions about the impact of the intervention on patients, the purpose was to explore feasibility. It was not possible to involve any employers in the study. Therefore, uptake of recommendations from the employer's perspective is unknown.

Additional outputs and published analyses related to work package objectives

- Rai,¹¹⁶ shortlisted for the British Thoracic Society Early Career Investigator of the Year award (2013), with a 'highly commended' prize award.
- Rai *et al.*¹¹⁹ This systematic review (based on 44 studies published from 1937 to 2017) summarised the effects of COPD on employment and work productivity. The main findings were that people with COPD were less likely to be in paid employment than similar counterparts without COPD. There was also some evidence of poorer work productivity among people with COPD, although relatively few studies had examined the effect of disease on presenteeism. The limitations in the current evidence were highlighted, with recommendations for future research.

Patient and public involvement

Patient advisory group

Patient involvement has been a central part of this programme from the planning stage. From the start, we involved a patient with COPD (Michael Darby) who was the former chairperson of the Birmingham 'Breathe Easy' patient group and has advised on previous research studies. In discussion with him, we planned to set up a small panel of patients [the patient advisory group (PAG)] chaired by MD. MD was also invited to the external programme steering committee meetings and wider investigator meetings.

Prior to submission of the proposal, MD contributed to the programme plans by advising on the following aspects:

- the need for clear and simple patient information leaflets, with a suggestion that these are read through and commented on by the PAG
- the potential problem of incomplete response rates to mailed questionnaires and the suggestion of obtaining data through additional sources if possible (leading to us supplementing data collection by use of EHRs)
- highlighting potential ill health among the PAG and suggesting a deputy chairperson to support the role.

The PAG was formed once the programme started and five individuals with COPD were appointed. Over the course of the programme, the group met five times, with additional support in between to comment on documents and meetings with other researchers to discuss new project ideas. Each meeting was attended by at least three PAG members and lasted for around 2 to 3 hours. A charter with terms of reference was drawn up and agreed, and PAG members were provided with some initial training at the first meeting.

The PAG provided input to the following aspects of the programme:

- commenting on and modifying wording for the patient information leaflets
- suggestions for improving the wording and flow of questionnaires and how these were grouped
- piloting completion of questionnaires to provide an estimate of timing
- piloting the patient assessment process and advising on how to organise the assessments
- advising on practical issues that patients would face when attending assessments and how to support patient attendance
- ensuring that we included an opt-out process for patients who may not want their data accessed through the practice as part of the TargetCOPD follow-up study.

At each meeting, PAG members received an update on the programme and the findings so far and had an opportunity to reflect and comment. Mostly, this resulted in general approval and support of the findings, with no modifications.

The PAG has been consulted about the dissemination of findings and has suggested that an opportunity to invite patients to an open evening with interesting speakers, reports on the findings and a social element (preferably in spring) would be welcome.

Multistory

During the course of the programme we were approached by an arts-based charity, Multistory (URL: <https://multistory.org.uk>; accessed 31 August), who had commissioned an artist to undertake a project (Black Country Lungs) to describe the story of people with COPD in the Black Country.¹²⁰ The charity approached us based on the BLISS research programme from a website search. They used a discussion on the various themes in the programme and our findings as a basis for exploring ideas with patients who took part in their project.

In addition to their main exhibition, a preview of artwork was displayed at the University of Birmingham Science and Art Exhibition, where members of the public and participants from our research study were invited. Our research group was involved in a panel discussion at which we summarised the findings from our programme.¹²¹

Conclusions and research recommendations

Screening for undiagnosed chronic obstructive pulmonary disease

Underdiagnosis of COPD is well recognised worldwide, with at least half of patients thought to be undiagnosed.¹²² Although there is some evidence that, overall, these individuals consume health services to an equivalent degree to those with diagnosed disease,¹²³ there is insufficient evidence that screening for undiagnosed COPD is worthwhile.^{46,124,125} One common uncertainty is the lack of trial evidence that the early identification of COPD leads to clinical benefits.

Our systematic reviews of studies of case-finding have shown that targeting screening to a higher-risk group is important¹²⁶ and identified which of the currently tested screening strategies is/are most effective in increasing yield.⁵¹ The TargetCOPD trial demonstrated that case-finding for undiagnosed COPD is a cost-effective process for increasing the number of new COPD cases identified with much higher yield than routine practice, particularly if using an active, targeted approach.²¹ Furthermore, we have used data from the trial to develop alternative algorithms for case-finding that may improve the efficiency of the process further by reducing the number needed to screen.⁴⁹

The majority of newly identified cases in the TargetCOPD trial had potential to benefit from evidence-based recommended treatments. Using the best available evidence from the literature for our assumptions, our economic model demonstrated that a systematic, 3-yearly screening programme is likely to be cost-effective, with favourable cost/QALY gained in all scenarios (paper under review). We also found that case-finding was generally acceptable to patients⁴² and primary care staff,⁴³ although a lack of awareness in relation to symptoms (among patients) and approaches to effective management of early disease (among health-care staff), as well as limited resources to deal with increasing numbers of people with COPD, were highlighted by both groups.

Longer-term follow-up of patients who were case-found through our trial demonstrated that just over one in five were added to the practice COPD register and, even among these patients, guideline-recommended management was rarely administered. This may be related to the concerns raised in our qualitative study around low awareness of management of early COPD, lack of resources and perceived lack of effective strategies.

After 4 years' follow-up, we demonstrated no evidence that screening had an effect on clinical outcomes. Hospitalisation and mortality rates did not significantly differ between patients in the case-finding or routine care practices. Although respiratory hospitalisation rates were significantly higher in the active than in the opportunistic case-finding arm, there was no significant difference between groups in overall hospitalisation or mortality. This may be related to more hospitalisations being attributed to a respiratory cause in these patients who had a COPD diagnosis.

This finding may seem to contrast with the findings from our Markov model, which suggest that estimates of cost-effectiveness are robust as long as 8% of screen-detected patients are optimally treated. However, considering the small number of case-found patients added to the COPD register, the low levels of implementation of treatment and the probably reduced benefits of such treatment among more mildly affected patients could take the effective benefit of case-finding in our patient population below 8%.

Implications for screening

The lack of observed effects of case-finding on clinical outcomes in our trial could be related to a number of factors. First, we had a very low level of uptake of screening overall. Less than 40% of eligible patients responded to the initial screening questionnaire. Low levels of awareness of symptoms, lack of perceived susceptibility, fear of screening or greater importance being attached to competing comorbidities may explain this. Further research is needed to identify approaches for increasing uptake if a population screening programme is to be implemented.

Second, we found poor management of screen-detected COPD cases, with relatively few of them being added to the practice COPD register, with subsequent reviews and initiation of evidence-based interventions. Interviews with primary health-care staff around perceptions of screening highlighted fears around workload implications and overdiagnosis and the need for better training on how to manage screen-detected COPD. Further research should focus on the development and evaluation of pathways of care for screen-detected COPD cases. Furthermore, there is a need for prioritisation of resources to increase the capacity of primary care staff to deal with an influx of new COPD cases and the development of training programmes to support better management of people with COPD.

Third, we assumed that screen-detected COPD patients are the same as clinically diagnosed patients, with similar natural history of disease and with the same response to interventions. This assumption needs to be tested in future research. Follow-up of case-found patients is important to understand disease progression better over time. Furthermore, clinical trials should test the effectiveness of current therapies in case-found populations to assess whether or not they are as effective in these patients.

Overall, our findings are in keeping with the recommendations by the UK National Screening Committee^{43,44} and the USPSTF⁴⁵ that screening for undiagnosed COPD should not currently be implemented. The research recommended above will help support future decision-making. Although in this report, and in common with many respiratory researchers, we frequently use the word 'case-finding', where case-finding is undertaken in a systematic way it is a form of screening and, therefore, should be subject to the same criteria before being implemented.

Multidimensional prognostic model for chronic obstructive pulmonary disease

People with COPD have high risk of respiratory infections resulting in hospitalisation and also a higher risk of premature mortality than those without COPD. However, COPD is heterogeneous and not all patients progress in the same way. Traditionally, lung function has been used to grade COPD severity, but there is increasing evidence that prognosis is determined by an inter-related set of factors, which has led to the development of multidimensional prognostic models.¹²⁷ Existing models have predominantly been developed in secondary care populations and are mainly developed to predict mortality risk; few have been developed using high-quality statistical approaches or been externally validated, and they often do not perform better than measures of lung function alone.^{78,127,128} The most recent NICE guidelines³¹ highlight the need for prognostic tools that are validated in UK primary care COPD populations and that examine outcomes wider than just mortality.

We externally validated the ADO score, which was identified as the most discriminatory for 3-year mortality in a systematic review, in a UK primary care population.⁷⁸ Although we found that it has promising discrimination, the model needs to be recalibrated if used to predict risk of mortality within 1 to 2 years.

We also developed a new prognostic index to predict 2-year risk of hospitalisation for people with COPD in primary care. Our new BLISS model, which includes variables that are easily available in primary care settings, has promising discrimination and was adjusted for overfitting to help ensure calibration is more reliable in case-found individuals.

Further work is needed to externally validate the BLISS prognostic index. Further research is also needed to evaluate the use of the index to classify people with COPD into higher- and lower-risk groups to aid management decisions.

Occupational outcomes in chronic obstructive pulmonary disease

A high proportion of people with COPD are of working age, but they have poorer rates of employment and poor work productivity compared with those without COPD. To our knowledge, this was the first study to examine which factors are associated with occupational outcomes among people with COPD. We found that increasing breathlessness, disease progression (increasing number of respiratory hospital admissions rather than lung function decline) and greater occupational exposure to VGDF were associated with poorer work productivity. These disease-related factors were more likely to be associated with poor work productivity than sociodemographic and lifestyle factors. Our findings suggest that there may be a continuum from presenteeism to absenteeism to loss of employment.

Although our OH-focused intervention was not feasible, modifiable workplace adaptations and self-management actions were identified for almost all participants, suggesting possible benefit from such assessments in a different context.

Further research is needed to examine how presenteeism and absenteeism are related to better understand presenteeism in relation to health and to assess whether or not interventions to modify the course of COPD have an impact on occupational outcomes.

Summary of research recommendations

Screening

1. Development and evaluation of interventions to better implement effective treatments for COPD in primary care, including pathways to manage case-found COPD.
2. Evaluation of existing interventions in case-found COPD to determine if the interventions have similar effectiveness.
3. Long-term follow-up of TargetCOPD participants to establish whether or not clinical benefits might occur, given that people with case-found disease had milder symptoms and better lung function than those already on GP practice COPD registers. Development and evaluation of approaches for increasing uptake of invitation for screening for undiagnosed COPD.
4. Development of more efficient approaches to case-finding and identifying which screening test or strategy has the best performance (in terms of sensitivity and specificity).
5. Development and evaluation of different models for delivery of quality-assured diagnostic spirometry screening services, considering workforce implications and how this could be incorporated into the new early diagnostic hubs for primary care networks proposed in the long-term plan.

Prognosis

6. Description of natural history and prognosis of case-found patients and those with indicative symptoms but normal lung function, describing any heterogeneity, and establishing whether or not there are phenotypic characteristics that are associated with progression.
7. Exploration of how prognostic models might be used by primary care staff in managing COPD patients.
8. Evaluation of the BLISS prognostic model in directing patient management.
9. Validation of the BLISS case-finding algorithm.
10. External validation of the impact of the BLISS prognostic model.
11. Consideration of the development of new prognostic scores for primary care COPD patients that predict all-cause (rather than respiratory) hospitalisation, given the multimorbid nature of the condition.

Work-related impacts

12. Examination of the relationship between presenteeism and absenteeism and whether or not presenteeism has an impact on health-related outcomes.
13. Development and evaluation of interventions to reduce dyspnoea and VGDF exposure in occupational outcomes in people with COPD.
14. Codevelopment and evaluation of an OH intervention to improve work productivity among people with COPD who are in paid employment.

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The programme management group (Peymané Adab, Rachel Jordan, David Fitzmaurice, Alexandra Enocson and Andrew Dickens) met weekly to oversee programme progress, with contributions from other co-investigators and researchers at different stages of the programme. In addition to specific contributions outlined below, all authors have contributed to drafting or revising sections of this report and have approved the final submitted version.

Contributions of authors

Peymané Adab (<https://orcid.org/0000-0001-9087-3945>) (Professor of Public Health and Chronic Disease Epidemiology) co-designed the programme, wrote the initial proposal with support from other co-investigators, co-led the programme, oversaw the cohort WP and wrote the first draft of the final report. She was a member of the programme management committee and the external steering committee.

Rachel E Jordan (<https://orcid.org/0000-0002-0747-6883>) (Reader in Epidemiology) co-designed the programme, supported leading the programme, led and oversaw the TargetCOPD trial and wrote sections of the final report. She was a member of the programme management committee and the external steering committee.

David Fitzmaurice (<https://orcid.org/0000-0002-9104-6252>) (Professor of General Practice) co-led the programme and advised on GP practice recruitment and clinical aspects of the TargetCOPD trial. He was a member of the programme management committee and contributed to the external steering committee.

Jon G Ayres (<https://orcid.org/0000-0002-3163-3674>) (Professor of Environmental and Respiratory Medicine) conceived WP3 and initially oversaw this WP.

KK Cheng (<https://orcid.org/0000-0002-1516-1857>) (Professor of Public Health and Primary Care) contributed to the programme design and to writing the initial proposal. He advised on epidemiological aspects of the programme.

Brendan G Cooper (<https://orcid.org/0000-0003-0785-1038>) (Consultant Clinical Scientist) provided advice on physiological measurements and oversaw the spirometry training and quality control for the programme.

Amanda Daley (<https://orcid.org/0000-0002-4866-8726>) (Professor of Behavioural Medicine) advised on aspects of questionnaire design and PA assessment.

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Andrew Dickens (<https://orcid.org/0000-0002-7591-8129>) (Research Fellow) co-ordinated the cohort study and, in the final year, the overall programme. He sat on the management committee and contributed to all aspects of the programme.

Alexandra Enocson (<https://orcid.org/0000-0002-4415-0989>) (Programme Manager) co-ordinated the programme, ensuring all governance aspects were in place and managing the research team undertaking fieldwork. She managed the research team and led the analysis for the qualitative study to explore patients' views of case-finding. She also sat on the programme management committee.

Sheila Greenfield (<https://orcid.org/0000-0002-8796-4114>) (Professor of Medical Sociology) advised on and oversaw the qualitative aspects of the programme.

Shamil Haroon (<https://orcid.org/0000-0002-0096-1413>) (Academic Clinical Lecturer in Public Health and GP trainee) undertook systematic reviews of case-finding, led the analysis and writing up of the audit of management of case-found COPD patients, undertook and analysed the qualitative study to explore the views of health professionals and undertook the analysis and writing up of the BLISS case-finding algorithm.

Kate Jolly (<https://orcid.org/0000-0002-6224-2115>) (Professor of Public Health and Primary Care) advised on all aspects of the programme and contributed to questionnaire design and interpretation of the findings. She also contributed to the design of the qualitative elements of the programme and PA assessment.

Sue Jowett (<https://orcid.org/0000-0001-8936-3745>) (Reader in Health Economics) oversaw the design, analysis and writing up of the health economic aspects of the programme. She mentored the health economists who undertook analysis.

Tosin Lambe (<https://orcid.org/0000-0002-6229-2454>) (Health Service Researcher and Health Economic Modeller) undertook the main analysis for the health economic model in WP1 and commented on the final report.

James Martin (<https://orcid.org/0000-0002-0847-0985>) (Lecturer in Medical Statistics) undertook statistical analysis for all WPs under the supervision of Alice Sitch and contributed to interpretation of the findings.

Martin R Miller (<https://orcid.org/0000-0001-9971-5759>) (Honorary Professor of Medicine) advised on clinical aspects of the programme, designed the programme for quality control of spirometry and advised on measures of lung function to be included in the prognostic model.

Kiran Rai (<https://orcid.org/0000-0002-3250-0275>) (Research Fellow) designed, contributed to data collection, analysed and wrote all elements of WP3, under the supervision of Jon Ayres, Rachel Jordan and Peymané Adab. She contributed to other aspects of the programme and, in the final years, was part of the programme management committee.

Richard D Riley (<https://orcid.org/0000-0001-8699-0735>) (Professor of Biostatistics) advised on the design and analysis of the trial in WP1 and the prognostic model in WP2.

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Robert A Stockley (<https://orcid.org/0000-0003-3726-1207>) (Professor of Medicine) provided clinical expertise and advised on interpretation of findings in the programme.

Alice Turner (<https://orcid.org/0000-0002-5947-3254>) (Reader and Consultant in Respiratory Medicine) advised on clinical aspects of the programme, including the inputs for the health economics model. She advised on all aspects of the programme.

Contributions of others

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Publications

Lambe T, Adab P, Jordan RE, Sitch A, Enocson A, Jolly K, *et al.* Model-based evaluation of the long-term cost-effectiveness of systematic case-finding for COPD in primary care. *Thorax* 2019;**74**:730–9.

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Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

References

1. Ntritsos G, Franek J, Belbasis L, Christou MA, Markozannes G, Altman P, *et al*. Gender-specific estimates of COPD prevalence: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2018;**13**:1507–14. <https://doi.org/10.2147/COPD.S146390>
2. Adeloye D, Chua S, Lee C, Basquill C, Papan A, Theodoratou E, *et al*. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. *J Glob Health* 2015;**5**:020415. <https://doi.org/10.7189/jogh.05-020415>
3. Jordan RE, Lam KB, Cheng KK, Miller MR, Marsh JL, Ayres JG, *et al*. Case finding for chronic obstructive pulmonary disease: a model for optimising a targeted approach. *Thorax* 2010;**65**:492–8. <https://doi.org/10.1136/thx.2009.129395>
4. Martinez CH, Mannino DM, Jaimes FA, Curtis JL, Han MK, Hansel NN, Diaz AA. Undiagnosed obstructive lung disease in the United States. Associated factors and long-term mortality. *Ann Am Thorac Soc* 2015;**12**:1788–95. <https://doi.org/10.1513/AnnalsATS.201506-388OC>
5. Rennard SI, Vestbo J. Natural histories of chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2008;**5**:878–83. <https://doi.org/10.1513/pats.200804-035QC>
6. Rennard SI, Vestbo J. The many ‘small COPDs’: COPD should be an orphan disease. *Chest* 2008;**134**:623–7. <https://doi.org/10.1378/chest.07-3059>
7. Roche N, Dalmy F, Perez T, Kuntz C, Vergnenègre A, Neukirch F, *et al*. Impact of chronic airflow obstruction in a working population. *Eur Respir J* 2008;**31**:1227–33. <https://doi.org/10.1183/09031936.00089607>
8. Britton M. The burden of COPD in the UK: results from the confronting COPD survey. *Respir Med* 2003;**97**:S71–9. [https://doi.org/10.1016/S0954-6111\(03\)80027-6](https://doi.org/10.1016/S0954-6111(03)80027-6)
9. Schultz AB, Edington DW. Employee health and presenteeism: a systematic review. *J Occup Rehabil* 2007;**17**:547–79. <https://doi.org/10.1007/s10926-007-9096-x>
10. Mahon B, Bartlett C, Isojärvi J, Edwards M, Glanville J. *Literature Review: The Economic Costs of Lung Disease and the Cost Effectiveness of Policy and Service Interventions*. York: York Health Economics Consortium on behalf of the British Lung Foundation (BLF) and the British Thoracic Society; 2017.
11. McLean S, Hoogendoorn M, Hoogenveen RT, Feenstra TL, Wild S, Simpson CR, *et al*. Projecting the COPD population and costs in England and Scotland: 2011 to 2030. *Sci Rep* 2016;**6**:31893. <https://doi.org/10.1038/srep31893>
12. Trueman D, Woodcock F, Hancock E. *Estimating the Economic Burden of Respiratory Illness in the UK*. London: British Lung Foundation; 2017.
13. Ford ES, Murphy LB, Khavjou O, Giles WH, Bolt JB, Croft JB. Total and state-specific medical and absenteeism costs of COPD among adults aged 18 years in the United States for 2010 and projections through 2020. *Chest* 2015;**147**:31–45. <https://doi.org/10.1378/chest.14-0972>
14. Gibson GJ, Loddenkemper R, Lundbäck B, Sibille Y. Respiratory health and disease in Europe: the new European Lung White Book. *Eur Respir J* 2013;**42**:559–63. <https://doi.org/10.1183/09031936.00105513>
15. Kohansal R, Soriano JB, Agusti A. Investigating the natural history of lung function: facts, pitfalls, and opportunities. *Chest* 2009;**135**:1330–41. <https://doi.org/10.1378/chest.08-1750>

16. U.S. Preventive Services Task Force. Screening for chronic obstructive pulmonary disease using spirometry: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008;**148**:529–34. <https://doi.org/10.7326/0003-4819-148-7-200804010-00212>
17. Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. *Lancet* 2009;**374**:721–32. [https://doi.org/10.1016/S0140-6736\(09\)61290-3](https://doi.org/10.1016/S0140-6736(09)61290-3)
18. Han MK, Quibrera PM, Carretta EE, Barr RG, Bleecker ER, Bowler RP, *et al.* Frequency of exacerbations in patients with chronic obstructive pulmonary disease: an analysis of the SPIROMICS cohort. *Lancet Respir Med* 2017;**5**:619–26. [https://doi.org/10.1016/S2213-2600\(17\)30207-2](https://doi.org/10.1016/S2213-2600(17)30207-2)
19. Alahmari AD, Kowlessar BS, Patel AR, Mackay AJ, Allinson JP, Wedzicha JA, Donaldson GC. Physical activity and exercise capacity in patients with moderate COPD exacerbations. *Eur Respir J* 2016;**48**:340–9. <https://doi.org/10.1183/13993003.01105-2015>
20. Karch A, Vogelmeier C, Welte T, Bals R, Kauczor HU, Biederer J, *et al.* The German COPD cohort COSYCONET: aims, methods and descriptive analysis of the study population at baseline. *Respir Med* 2016;**114**:27–37. <https://doi.org/10.1016/j.rmed.2016.03.008>
21. Jordan RE, Adab P, Sitch A, Enocson A, Blissett D, Jowett S, *et al.* Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial. *Lancet Respir Med* 2016;**4**:720–30. [https://doi.org/10.1016/S2213-2600\(16\)30149-7](https://doi.org/10.1016/S2213-2600(16)30149-7)
22. Department of Health and Social Care (DHSC). *An Outcomes Strategy for Chronic Obstructive Pulmonary Disease (COPD) and Asthma in England*. London: DHSC; 2011.
23. British Lung Foundation. *Invisible Lives: Chronic Obstructive Pulmonary Disease (COPD) – Finding the Missing Millions*. London: British Lung Foundation; 2007. URL: <https://lunguk.org/NR/rdonlyres/E027CA18-B5C6-49AB-96FA-C4AF55E6F484/0/InvisibleLivesreport.pdf> (accessed 21 April 2021).
24. Frank TL, Hazell ML, Linehan MF, Frank PI. The diagnostic accuracies of chronic obstructive pulmonary disease (COPD) in general practice: the results of the MAGIC (Manchester Airways Group Identifying COPD) study. *Prim Care Respir J* 2006;**15**:286–93. <https://doi.org/10.1016/j.pcrj.2006.07.007>
25. Tinkelman DG, Price DB, Nordyke RJ, Halbert RJ. COPD screening efforts in primary care: what is the yield? *Prim Care Respir J* 2007;**16**:41–8. <https://doi.org/10.3132/pcrj.2007.00009>
26. Bednarek M, Maciejewski J, Wozniak M, Kuca P, Zielinski J. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax* 2008;**63**:402–7. <https://doi.org/10.1136/thx.2007.085456>
27. Buffels J, Degryse J, Heyrman J, Decramer M, DIDASCO Study. Office spirometry significantly improves early detection of COPD in general practice: the DIDASCO Study. *Chest* 2004;**125**:1394–9. <https://doi.org/10.1378/chest.125.4.1394>
28. Van Schayck CP, Loozen JM, Wagena E, Akkermans RP, Wesseling GJ. Detecting patients at a high risk of developing chronic obstructive pulmonary disease in general practice: cross sectional case finding study. *BMJ* 2002;**324**:1370. <https://doi.org/10.1136/bmj.324.7350.1370>
29. Vandevoorde J, Verbanck S, Gijssels L, Schuermans D, Devroey D, De Backer J, *et al.* Early detection of COPD: a case finding study in general practice. *Respir Med* 2007;**101**:525–30. <https://doi.org/10.1016/j.rmed.2006.06.027>
30. Wilt TJ, Niewoehner D, MacDonald R, Kane RL. Management of stable chronic obstructive pulmonary disease: a systematic review for a clinical practice guideline. *Ann Intern Med* 2007;**147**:639–53. <https://doi.org/10.7326/0003-4819-147-9-200711060-00009>

31. National Institute for Health and Care Excellence (NICE). *Chronic Obstructive Pulmonary Disease in Over 16s: Diagnosis and Management*. NICE guideline [NG115]. London: NICE; 2010.
32. Curtis LA, Burns A. *Unit Costs of Health and Social Care 2013*. Canterbury: Personal Social Services Research Unit, University of Kent; 2013.
33. National Institute for Health Research. *NIHR Costing Report*. URL: www.crn.nihr.ac.uk/resources/resource-template/ (accessed 11 August 2015).
34. Jordan RE, Adab P, Sitch A, Enocson A, Blissett D, Jowett S, *et al*. Supplementary appendix. Supplement to: Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial. *Lancet Respir Med* 2016;4:P720–30.
35. Lambe T, Adab P, Jordan RE, Sitch A, Enocson A, Jolly K, *et al*. Model-based evaluation of the long-term cost-effectiveness of systematic case-finding for COPD in primary care. *Thorax* 2019;74:730–9. <https://doi.org/10.1136/thoraxjnl-2018-212148>
36. Dretzke J, Blissett D, Dave C, Mukherjee R, Price M, Bayliss S, *et al*. The cost-effectiveness of domiciliary non-invasive ventilation in patients with end-stage chronic obstructive pulmonary disease: a systematic review and economic evaluation. *Health Technol Assess* 2015;19(81). <https://doi.org/10.3310/hta19810>
37. Ramsey SD, Sullivan SD. The burden of illness and economic evaluation for COPD. *Eur Respir J* 2003;41:29s–35s. <https://doi.org/10.1183/09031936.03.00078203>
38. National Institute for Health and Care Excellence (NICE). *Chronic Obstructive Pulmonary Disease: Costing Report – Implementing NICE Guidance*. London: NICE; 2011.
39. Curtis LA, Burns A. *Unit Costs of Health and Social Care 2015*. Canterbury: Personal Social Services Research Unit, University of Kent; 2015.
40. Karner C, Chong J, Poole P. Tiotropium versus placebo for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2014;7:CD009285. <https://doi.org/10.1002/14651858.CD009285.pub3>
41. Nannini LJ, Poole P, Milan SJ, Holmes R, Normansell R. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus placebo for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013;11:CD003794. <https://doi.org/10.1002/14651858.CD003794.pub4>
42. Enocson A, Jolly K, Jordan RE, Fitzmaurice DA, Greenfield SM, Adab P. Case-finding for COPD in primary care: a qualitative study of patients' perspectives. *Int J Chron Obstruct Pulmon Dis* 2018;13:1623–32. <https://doi.org/10.2147/COPD.S147718>
43. Haroon S, Jordan RE, Fitzmaurice DA, Adab P. Case finding for COPD in primary care: a qualitative study of the views of health professionals. *Int J Chron Obstruct Pulmon Dis* 2015;10:1711–18. <https://doi.org/10.2147/COPD.S84247>
44. UK National Screening Committee (UK NSC). *UK NSC Policy on Chronic Obstructive Pulmonary Disease*. London: UK NSC; 2013.
45. Cartwright S. *An Evaluation of Screening for COPD Against the National Screening Committee Criteria*. London: Public Health England; 2012.
46. Guirguis-Blake JM, Senger CA, Webber EM, Mularski RA, Whitlock EP. Screening for chronic obstructive pulmonary disease: evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2016;315:1378–93. <https://doi.org/10.1001/jama.2016.2654>

47. Jordan RE, Adab P, Jowett S, Marsh JL, Riley RD, Enocson A, *et al*. TargetCOPD: a pragmatic randomised controlled trial of targeted case finding for COPD versus routine practice in primary care: protocol. *BMC Pulm Med* 2014;**14**:157. <https://doi.org/10.1186/1471-2466-14-157>
48. Miller MR, Haroon S, Jordan RE, Sitch AJ, Dickens AP, Enocson A, *et al*. Clinical characteristics of patients newly diagnosed with COPD by the fixed ratio and lower limit of normal criteria: a cross-sectional analysis of the TargetCOPD trial. *Int J Chron Obstruct Pulmon Dis* 2018;**13**:1979–86. <https://doi.org/10.2147/COPD.S146914>
49. Haroon S, Adab P, Riley RD, Fitzmaurice D, Jordan RE. Predicting risk of undiagnosed COPD: development and validation of the TargetCOPD score. *Eur Respir J* 2017;**49**:1602191. <https://doi.org/10.1183/13993003.02191-2016>
50. Haroon S, Adab P, Riley RD, Marshall T, Lancashire R, Jordan RE. Predicting risk of COPD in primary care: development and validation of a clinical risk score. *BMJ Open Respir Res* 2015;**2**:e000060. <https://doi.org/10.1136/bmjresp-2014-000060>
51. Haroon SM, Jordan RE, O'Beirne-Elliman J, Adab P. Effectiveness of case finding strategies for COPD in primary care: a systematic review and meta-analysis. *NPJ Prim Care Respir Med* 2015;**25**:15056. <https://doi.org/10.1038/npjpcrm.2015.56>
52. Haroon S, Jordan R, Takwoingi Y, Adab P. Diagnostic accuracy of screening tests for COPD: a systematic review and meta-analysis. *BMJ Open* 2015;**5**:e008133. <https://doi.org/10.1136/bmjopen-2015-008133>
53. Adab P, Fitzmaurice DA, Dickens AP, Ayres JG, Buni H, Cooper BG, *et al*. Cohort profile: the Birmingham Chronic Obstructive Pulmonary Disease (COPD) Cohort Study. *Int J Epidemiol* 2017;**46**:23. <https://doi.org/10.1093/ije/dyv350>
54. Donaldson GC, Seemungal TA, Patel IS, Bhowmik A, Wilkinson TM, Hurst JR, *et al*. Airway and systemic inflammation and decline in lung function in patients with COPD. *Chest* 2005;**128**:1995–2004. <https://doi.org/10.1378/chest.128.4.1995>
55. Vestbo J, Anderson W, Coxson HO, Crim C, Dawber F, Edwards L, *et al*. Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (ECLIPSE). *Eur Respir J* 2008;**31**:869–73. <https://doi.org/10.1183/09031936.00111707>
56. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, *et al*. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 2004;**350**:1005–12. <https://doi.org/10.1056/NEJMoa021322>
57. Kohansal R, Martinez-Camblor P, Agustí A, Buist AS, Mannino DM, Soriano JB. The natural history of chronic airflow obstruction revisited: an analysis of the Framingham offspring cohort. *Am J Respir Crit Care Med* 2009;**180**:3–10. <https://doi.org/10.1164/rccm.200901-0047OC>
58. Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999;**160**:1856–61. <https://doi.org/10.1164/ajrccm.160.6.9902115>
59. Prescott E, Bjerg AM, Andersen PK, Lange P, Vestbo J. Gender difference in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. *Eur Respir J* 1997;**10**:822–7.
60. Yin P, Jiang CQ, Cheng KK, Lam TH, Lam KH, Miller MR, *et al*. Passive smoking exposure and risk of COPD among adults in China: the Guangzhou Biobank Cohort Study. *Lancet* 2007;**370**:751–7. [https://doi.org/10.1016/S0140-6736\(07\)61378-6](https://doi.org/10.1016/S0140-6736(07)61378-6)

61. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS, GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001;**163**:1256–76. <https://doi.org/10.1164/ajrccm.163.5.2101039>
62. Vestbo J, Lange P. Can GOLD stage 0 provide information of prognostic value in chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 2002;**166**:329–32. <https://doi.org/10.1164/rccm.2112048>
63. Mannino DM. GOLD stage 0 COPD: is it real? Does it matter? *Chest* 2006;**130**:309–10. [https://doi.org/10.1016/S0012-3692\(15\)51839-4](https://doi.org/10.1016/S0012-3692(15)51839-4)
64. de Marco R, Accordini S, Cerveri I, Corsico A, Antó JM, Künzli N, *et al.* Incidence of chronic obstructive pulmonary disease in a cohort of young adults according to the presence of chronic cough and phlegm. *Am J Respir Crit Care Med* 2007;**175**:32–9. <https://doi.org/10.1164/rccm.200603-381OC>
65. Mannino DM, Doherty DE, Sonia Buist A. Global initiative on Obstructive Lung Disease (GOLD) classification of lung disease and mortality: findings from the Atherosclerosis Risk in Communities (ARIC) study. *Respir Med* 2006;**100**:115–22. <https://doi.org/10.1016/j.rmed.2005.03.035>
66. Office for National Statistics. *Standard Occupational Classification 2010*. URL: www.ons.gov.uk/methodology/classificationsandstandards/standardoccupationalclassificationsoc/soc2010 (accessed 13 December 2019).
67. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009;**34**:648–54. <https://doi.org/10.1183/09031936.00102509>
68. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, *et al.* Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;**20**:1727–36. <https://doi.org/10.1007/s11136-011-9903-x>
69. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;**16**:606–13. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
70. Koopman C, Pelletier KR, Murray JF, Sharda CE, Berger ML, Turpin RS, *et al.* Stanford presenteeism scale: health status and employee productivity. *J Occup Environ Med* 2002;**44**:14–20. <https://doi.org/10.1097/00043764-200201000-00004>
71. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;**4**:353–65. <https://doi.org/10.2165/00019053-199304050-00006>
72. Keene SJ, Jordan RE, Franssen FM, de Vries F, Martin J, Sitch A, *et al.* External validation of the updated ADO score in COPD patients from the Birmingham COPD Cohort. *Int J Chron Obstruct Pulmon Dis* 2019;**14**:2395–407. <https://doi.org/10.2147/COPD.S212381>
73. Miller MR, Pedersen OF, Pellegrino R, Brusasco V. Debating the definition of airflow obstruction: time to move on? *Eur Respir J* 2009;**34**:527–8. <https://doi.org/10.1183/09031936.00103309>
74. Miller MR, Pedersen OF, Dirksen A. A new staging strategy for chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2007;**2**:657–63.
75. Miller MR, Pedersen OF. New concepts for expressing forced expiratory volume in 1 s arising from survival analysis. *Eur Respir J* 2010;**35**:873–82. <https://doi.org/10.1183/09031936.00025809>

76. Puhan MA, Garcia-Aymerich J, Frey M, ter Riet G, Antó JM, Agustí AG, *et al.* Expansion of the prognostic assessment of patients with chronic obstructive pulmonary disease: the updated BODE index and the ADO index. *Lancet* 2009;**374**:704–11. [https://doi.org/10.1016/S0140-6736\(09\)61301-5](https://doi.org/10.1016/S0140-6736(09)61301-5)
77. Dijk WD, Bemt Lv, Haak-Rongen Sv, Bischoff E, Weel Cv, Veen JC, Schermer TR. Multidimensional prognostic indices for use in COPD patient care: a systematic review. *Respir Res* 2011;**12**:151. <https://doi.org/10.1186/1465-9921-12-151>
78. Guerra B, Haile SR, Lamprecht B, Ramírez AS, Martínez-Cambolor P, Kaiser B, *et al.* Large-scale external validation and comparison of prognostic models: an application to chronic obstructive pulmonary disease. *BMC Med* 2018;**16**:33. <https://doi.org/10.1186/s12916-018-1013-y>
79. Smith LE, Moore E, Ali I, Smeeth L, Stone P, Quint JK. Prognostic variables and scores identifying the end of life in COPD: a systematic review. *Int J Chron Obstruct Pulmon Dis* 2017;**12**:2239–56. <https://doi.org/10.2147/COPD.S137868>
80. Soler-Cataluña JJ, Martínez-García MA, Sánchez LS, Tordera MP, Sánchez PR. Severe exacerbations and BODE index: two independent risk factors for death in male COPD patients. *Respir Med* 2009;**103**:692–9. <https://doi.org/10.1016/j.rmed.2008.12.005>
81. Esteban C, Quintana JM, Aburto M, Moraza J, Capelastegui A. A simple score for assessing stable chronic obstructive pulmonary disease. *QJM* 2006;**99**:751–9. <https://doi.org/10.1093/qjmed/hcl110>
82. Esteban C, Quintana JM, Aburto M, Moraza J, Arostegui I, España PP, *et al.* The health, activity, dyspnea, obstruction, age, and hospitalization: prognostic score for stable COPD patients. *Respir Med* 2011;**105**:1662–70. <https://doi.org/10.1016/j.rmed.2011.05.005>
83. Niewoehner DE, Lokhnygina Y, Rice K, Kuschner WG, Sharafkhaneh A, Sarosi GA, *et al.* Risk indexes for exacerbations and hospitalizations due to COPD. *Chest* 2007;**131**:20–8. <https://doi.org/10.1378/chest.06-1316>
84. Bertens LC, Reitsma JB, Moons KG, van Mourik Y, Lammers JW, Broekhuizen BD, *et al.* Development and validation of a model to predict the risk of exacerbations in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2013;**8**:493–9. <https://doi.org/10.2147/COPD.S49609>
85. Schembri S, Anderson W, Morant S, Winter J, Thompson P, Pettitt D, *et al.* A predictive model of hospitalisation and death from chronic obstructive pulmonary disease. *Respir Med* 2009;**103**:1461–7. <https://doi.org/10.1016/j.rmed.2009.04.021>
86. Miravittles M, Llor C, de Castellar R, Izquierdo I, Baró E, Donado E. Validation of the COPD severity score for use in primary care: the NEREA study. *Eur Respir J* 2009;**33**:519–27. <https://doi.org/10.1183/09031936.00087208>
87. Briggs A, Spencer M, Wang H, Mannino D, Sin DD. Development and validation of a prognostic index for health outcomes in chronic obstructive pulmonary disease. *Arch Intern Med* 2008;**168**:71–9. <https://doi.org/10.1001/archinternmed.2007.37>
88. Jones RC, Donaldson GC, Chavannes NH, Kida K, Dickson-Spillmann M, Harding S, *et al.* Derivation and validation of a composite index of severity in chronic obstructive pulmonary disease: the DOSE Index. *Am J Respir Crit Care Med* 2009;**180**:1189–95. <https://doi.org/10.1164/rccm.200902-0271OC>
89. Wyatt JC, Altman DG. Commentary: Prognostic models: clinically useful or quickly forgotten? *BMJ* 1995;**311**:1539–41. <https://doi.org/10.1136/bmj.311.7019.1539>

90. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;**49**:1373–9. [https://doi.org/10.1016/S0895-4356\(96\)00236-3](https://doi.org/10.1016/S0895-4356(96)00236-3)
91. Kosteli MC, Heneghan NR, Roskell C, Williams SE, Adab P, Dickens AP, *et al.* Barriers and enablers of physical activity engagement for patients with COPD in primary care. *Int J Chron Obstruct Pulmon Dis* 2017;**12**:1019–31. <https://doi.org/10.2147/COPD.S119806>
92. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am J Respir Crit Care Med* 2007;**175**:458–63. <https://doi.org/10.1164/rccm.200607-896OC>
93. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax* 2006;**61**:772–8. <https://doi.org/10.1136/thx.2006.060145>
94. Maltais F, Bourbeau J, Shapiro S, Lacasse Y, Perrault H, Baltzan M, *et al.* Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *Ann Intern Med* 2008;**149**:869–78. <https://doi.org/10.7326/0003-4819-149-12-200812160-00006>
95. Bolton CE, Bevan-Smith EF, Blakey JD, Crowe P, Elkin SL, Garrod R, *et al.* British Thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax* 2013;**68**(Suppl. 2):ii1–30. <https://doi.org/10.1136/thoraxjnl-2013-203808>
96. Johnston K, Grimmer-Somers K. Pulmonary rehabilitation: overwhelming evidence but lost in translation? *Physiother Can* 2010;**62**:368–73. <https://doi.org/10.3138/physio.62.4.368>
97. Buni H. *The Relevance of Chronic Respiratory Symptoms Without Airflow Obstruction: Health-Related Characteristics and Impact on Patient Prognosis*. PhD thesis. Birmingham: University of Birmingham; 2016. URL: <http://etheses.bham.ac.uk/6699/>
98. Lopez-Campos JL, Alcazar B. Evaluation of symptomatic patients without airflow obstruction: back to the future. *J Thorac Dis* 2016;**8**:E1657–60. <https://doi.org/10.21037/jtd.2016.12.103>
99. NatCen Social Research and Royal Free and University College Medical School Department of Epidemiology and Public Health. *Health Survey for England, 2010* [computer file]. Colchester: UK Data Archive; 2012.
100. Brien SB, Stuart B, Dickens AP, Kendrick T, Jordan RE, Adab P, Thomas M. Independent determinants of disease-related quality of life in COPD – scope for nonpharmacologic interventions? *Int J Chron Obstruct Pulmon Dis* 2018;**13**:247–56. <https://doi.org/10.2147/copd.s152955>
101. Jolly K, Sidhu MS, Hewitt CA, Coventry PA, Daley A, Jordan R, *et al.* Self management of patients with mild COPD in primary care: randomised controlled trial. *BMJ* 2018;**361**:k2241. <https://doi.org/10.1136/bmj.k2241>
102. Dickens A, Fitzmaurice D, Adab P, Sitch A, Riley RD, Enocson A, Jordan R. Accuracy of Vitalograph lung monitor as a screening test for COPD in primary care. *NPJ Prim Care Respir Med* 2020;**30**:1–8. <https://doi.org/10.1038/s41533-019-0158-2>
103. Khan A, Dickens AP, Adab P, Jordan RE. Self-management behaviour and support among primary care COPD patients: cross-sectional analysis of data from the Birmingham Chronic Obstructive Pulmonary Disease Cohort. *NPJ Prim Care Respir Med* 2017;**27**:46. <https://doi.org/10.1038/s41533-017-0046-6>
104. Kosteli MC. *Imagery Use in Older Adults*. PhD thesis. Birmingham: University of Birmingham; 2016. URL: <http://etheses.bham.ac.uk/6780/>

REFERENCES

105. Rai KK, Jordan RE, Siebert WS, Sadhra SS, Fitzmaurice DA, Sitch AJ, *et al.* Birmingham COPD Cohort: a cross-sectional analysis of the factors associated with the likelihood of being in paid employment among people with COPD. *Int J Chron Obstruct Pulmon Dis* 2017;**12**:233–42. <https://doi.org/10.2147/COPD.S119467>
106. Rai KK, Adab P, Ayres JG, Siebert WS, Sadhra SS, Sitch AJ, *et al.* Factors associated with work productivity among people with COPD: Birmingham COPD Cohort. *Occup Environ Med* 2017;**74**:859–67. <https://doi.org/10.1136/oemed-2016-104014>
107. Britton M. The burden of COPD in the UK: results from the Confronting COPD survey. *Respir Med* 2003;**97**(Suppl. C):71–9. [https://doi.org/10.1016/S0954-6111\(03\)80027-6](https://doi.org/10.1016/S0954-6111(03)80027-6)
108. Schultz AB, Edington DW. Employee health and presenteeism: a systematic review. *J Occup Rehabil* 2007;**17**:547–79. <https://doi.org/10.1007/s10926-007-9096-x>
109. Roche N, Dalmay F, Perez T, Kuntz C, Vergnenègre A, Neukirch F, *et al.* Impact of chronic airflow obstruction in a working population. *Eur Respir J* 2008;**31**:1227–33. <https://doi.org/10.1183/09031936.00089607>
110. Sin DD, Stafinski T, Ng YC, Bell NR, Jacobs P. The impact of chronic obstructive pulmonary disease on work loss in the United States. *Am J Respir Crit Care Med* 2002;**165**:704–7. <https://doi.org/10.1164/ajrccm.165.5.2104055>
111. Yelin E, Katz P, Balmes J, Trupin L, Earnest G, Eisner M, Blanc P. Work life of persons with asthma, rhinitis, and COPD: a study using a national, population-based sample. *J Occup Med Toxicol* 2006;**1**:2. <https://doi.org/10.1186/1745-6673-1-2>
112. Collins JJ, Baase CM, Sharda CE, Ozminkowski RJ, Nicholson S, Billotti GM, *et al.* The assessment of chronic health conditions on work performance, absence, and total economic impact for employers. *J Occup Environ Med* 2005;**47**:547–57. <https://doi.org/10.1097/01.jom.0000166864.58664.29>
113. Kretschman D, Gao W, Dupuis J, Latourelle J, O'Connor G. Rate of FEV1 decline in healthy adults: defining the upper limit of normal in the Framingham Heart Study. *Am J Respir Crit Care Med* 2012;**185**:A2056. https://doi.org/10.1164/ajrccm-conference.2012.185.1_MeetingAbstracts.A2056
114. Mahler DA, Witek TJ. The MCID of the transition dyspnea index is a total score of one unit. *COPD* 2005;**2**:99–103. <https://doi.org/10.1081/copd-200050666>
115. Alma H, de Jong C, Jelusic D, Wittmann M, Schuler M, Flokstra-de Blok B, *et al.* Health status instruments for patients with COPD in pulmonary rehabilitation: defining a minimal clinically important difference. *NPJ Prim Care Respir Med* 2016;**26**:16041. <https://doi.org/10.1038/npjpcrm.2016.41>
116. Kalirai KK. *The Effects of Chronic Obstructive Pulmonary Disease on Work Related Outcomes.* PhD thesis. Birmingham: University of Birmingham; 2016. URL: <http://etheses.bham.ac.uk/6846/> (accessed 4 February 2020).
117. Black C. *Working for a Healthier Tomorrow: Work and Health in Britain.* London: Department for Work and Pensions; 2008.
118. Verbeek J, Madan I. From sick notes to fit notes. *BMJ* 2009;**339**:b3114. <https://doi.org/10.1136/bmj.b3114>
119. Rai KK, Adab P, Ayres JG, Jordan RE. Systematic review: chronic obstructive pulmonary disease and work-related outcomes. *Occup Med* 2018;**68**:99–108. <https://doi.org/10.1093/occmed/kqy012>

120. Multistory. *Black Country Lungs*. 2017. URL: <https://multistory.org.uk/project/black-country-lungs/> (accessed 5 December 2018).
121. University of Birmingham Arts & Science Festival. *Black Country Lungs: In Conversation*. 2018. URL: <https://artsandsciencefestival.co.uk/festival-event/black-country-lungs-in-conversation/> (accessed 5 December 2018).
122. Almagro P, Soriano JB. Underdiagnosis in COPD: a battle worth fighting. *Lancet Respir Med* 2017;**5**:367–8. [https://doi.org/10.1016/S2213-2600\(17\)30133-9](https://doi.org/10.1016/S2213-2600(17)30133-9)
123. Labonté LE, Tan WC, Li PZ, Mancino P, Aaron SD, Benedetti A, *et al*. Undiagnosed chronic obstructive pulmonary disease contributes to the burden of health care use. Data from the CanCOLD study. *Am J Respir Crit Care Med* 2016;**194**:285–98. <https://doi.org/10.1164/rccm.201509-1795OC>
124. UK National Screening Committee (UK NSC). *UK NSC Recommendation on Chronic Obstructive Pulmonary Disease*. London: UK NSC; 2018. URL: <https://legacyscreening.phe.org.uk/copd> (accessed 19 October 2018).
125. Lin K, Watkins B, Johnson T, Rodriguez JA, Barton MB, U.S. Preventive Services Task Force. Screening for chronic obstructive pulmonary disease using spirometry: summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008;**148**:535–43. <https://doi.org/10.7326/0003-4819-148-7-200804010-00213>
126. Haroon SM, Adab PA, Jordan RE. Case finding for COPD in primary care: a systematic review. *Prim Care Respir J* 2012;**21**:354–7. <https://doi.org/10.4104/pcrj.2012.00060>
127. Bellou V, Belbasis L, Konstantinidis A, Tzoulaki I, Evangelou E. A systematic review of prognostic models in COPD. *Eur Respir J* 2017;**50**(Suppl. 61):PA1565. <https://doi.org/10.1183/1393003.congress-2017.PA1565>
128. Guerra B, Gaveikaite V, Bianchi C, Puhan MA. Prediction models for exacerbations in patients with COPD. *Eur Respir Rev* 2017;**26**:160061. <https://doi.org/10.1183/16000617.0061-2016>

Appendix 1 List of publications arising from programme, with full-text links

Peer-reviewed papers (published)

Title	Journal	Authors	Year	Full text link
Accuracy of Vitalograph lung monitor as a screening test for COPD in primary care	<i>npj Primary Care Respiratory Medicine</i>	Dickens AP, Fitzmaurice DA, Adab P, Sitch A, Riley RD, Enocson A, Jordan RE	2019	
External validation of the updated ADO score in COPD patients from the Birmingham COPD cohort.	<i>International Journal of Chronic Obstructive Pulmonary Disease</i>	SJ Keene, RE Jordan, FME Franssen, F de Vries, J Martin, A Sitch, A Turner, AP Dickens, D Fitzmaurice, P Adab	2019	www.ncbi.nlm.nih.gov/pmc/articles/PMC6818100/
A model-based evaluation of the long-term cost-effectiveness of systematic case-finding for COPD in primary care	<i>Thorax</i>	Lambe T, Adab P, Jordan R, Sitch A, Enocson A, Jolly K, Marsh J, Riley RD, Miller MR, Cooper BG, Turner AM, Ayres J, Stockley R, Greenfield S, Siebert S, Daley A, Cheng KK, Fitzmaurice D, Jowett S	2019	http://doi.org/10.1136/thoraxjnl-2018-212148
Case-finding for COPD in Primary Care: A qualitative study of patients' perspectives	<i>International Journal of Chronic Obstructive Pulmonary Disease</i>	Enocson A, Jolly K, Jordan R, Fitzmaurice D, Greenfield S, Adab P, Cheng K, Cooper BG, Daley A, Dickens A, O'Beirne-Elliman J, Haroon S, Jowett S, Kalirai K, Marsh J, Miller MR, Riley R, Stockley R, Turner A	2018	https://doi.org/10.2147/COPD.S147718
Clinical characteristics of patients newly diagnosed with chronic obstructive pulmonary disease by the fixed ratio and lower limit of normal criteria: a cross-sectional analysis of the TargetCOPD trial	<i>International Journal of COPD</i>	MR Miller, S Haroon, RE Jordan, A Sitch, AP Dickens, A Enocson, DA Fitzmaurice, P Adab	2018	https://doi.org/10.2147/COPD.S146914
Systematic review: chronic obstructive pulmonary disease and work-related outcomes	<i>Occupational Medicine</i>	K K Rai, P Adab, J G Ayres, R E Jordan	2018	https://doi.org/10.1093/occmed/kqy012
Independent determinants of disease-related quality of life in COPD – scope for non-pharmacological interventions?	<i>International Journal of COPD</i>	Brien SB, Stuart B, Dickens AP, Kendrick T, Jordan RE, Adab P, Thomas M	2018	https://doi.org/10.2147/COPD.S152955
Factors associated with work productivity among people with COPD: Birmingham COPD Cohort	<i>Occupational and Environmental Medicine</i>	K Rai, R Jordan, JG Ayres, S Siebert, SS Sadhra, A Sitch, D Fitzmaurice, P Adab	2017	http://doi.org/10.1136/oemed-2016-104014
Self-management behaviour and support among primary care COPD patients: Cross-sectional analysis of data from the Birmingham Chronic Obstructive Pulmonary Disease Cohort	<i>npj Primary Care Respiratory Medicine</i>	A Khan, AP Dickens, P Adab, RE Jordan	2017	https://doi.org/10.1038/s41533-017-0046-6
Predicting risk of undiagnosed COPD in primary care: Development and validation of the TargetCOPD score	<i>European Respiratory Journal</i>	Haroon SMM, Adab P, Riley RD, Fitzmaurice D, Jordan RE	2017	https://doi.org/10.1183/13993003.02191-2016
Barriers and enablers of physical activity engagement for patients with chronic obstructive pulmonary disease (COPD) in primary care	<i>International Journal of COPD</i>	M-C Kosteli, N Heneghan, C Roskell, SE Williams, P Adab, AP Dickens, A Enocson, D Fitzmaurice, K Jolly, R Jordan, S Greenfield, J Cumming	2017	https://doi.org/10.2147/COPD.S119806

Title	Journal	Authors	Year	Full text link
Birmingham COPD Cohort: a cross-sectional analysis of the factors associated with the likelihood of being in paid employment among people with COPD	<i>International Journal of COPD</i>	KK Kalirai, RE Jordan, WS Siebert, SS Sadhra, DA Fitzmaurice, AJ Sitch, JG Ayres, P Adab	2016	https://doi.org/10.2147/COPD.S119467
Cohort Profile: The Birmingham Chronic Obstructive Pulmonary Disease (COPD) Cohort Study	<i>International Journal of Epidemiology</i>	P Adab, DA Fitzmaurice, AP Dickens, JG Ayres, H Buni, BG Cooper, AJ Daley, A Enocson, S Greenfield, K Jolly, S Jowett, K Kalirai, JL Marsh, MR Miller, RD Riley, WS Siebert, RA Stockley, AM Turner, KK Cheng, RE Jordan	2016	https://doi.org/10.1093/ije/dyv350
Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial	<i>Lancet Respiratory</i>	RE Jordan, P Adab, A Sitch, A Enocson, D Blissett, S Jowett, JL Marsh, RD Riley, MR Miller, BG Cooper, AM Turner, K Jolly, JG Ayres, S Haroon, RA Stockley, S Greenfield, S Siebert, A Daley, KK Cheng, D Fitzmaurice	2016	https://doi.org/10.1016/S2213-2600(16)30149-7
Predicting risk of COPD in primary care: development and validation of a clinical risk score	<i>BMJ Open Respiratory Research</i>	Haroon SMM, Adab P, Riley RD, Marshall T, Lancashire R, Jordan RE	2015	www.ncbi.nlm.nih.gov/pmc/articles/PMC4379885/
Case finding for COPD in primary care: a qualitative study of the views of health professionals	<i>International Journal of COPD</i>	Haroon S, Jordan RE, Fitzmaurice DA, Adab P	2015	https://doi.org/10.2147/COPD.S84247
Diagnostic accuracy of screening tests for COPD: a systematic review and meta-analysis	<i>BMJ Open Respiratory Research</i>	Haroon S, Jordan R, Takwoingi Y, Adab P	2015	https://doi.org/10.1136/bmjopen-2015-008133
Effectiveness of case finding strategies for COPD in primary care: a systematic review and meta-analysis	<i>NPJ Primary Care Respiratory Medicine</i>	Haroon SM, Jordan RE, O'Beirne-Elliman J, Adab P	2015	https://doi.org/10.1038/npjpcrm.2015.56
TargetCOPD: a pragmatic randomised controlled trial of targeted case finding for COPD versus routine practice in primary care: protocol	<i>BMC Pulmonary Medicine</i>	RE Jordan, P Adab, S Jowett, JL Marsh, RD Riley, A Enocson, MR Miller, BG Cooper, AM Turner, JG Ayres, KK Cheng, K Jolly, RA Stockley, S Greenfield, S Siebert, A Daley, D Fitzmaurice	2014	https://doi.org/10.1186/1471-2466-14-157
Case finding for chronic obstructive pulmonary disease in primary care: a pilot randomised controlled trial	<i>British Journal of General Practice</i>	Shamil Haroon, Peymane Adab, Carl Griffin, Rachel Jordan	2013	https://doi.org/10.3399/bjgp13x660788
Case finding for chronic obstructive pulmonary disease: a model for optimising a targeted approach	<i>Thorax</i>	Jordan RE, Cheng KK, Miller M, Marsh J, Ayres J, Fitzmaurice D, Adab P, Lam KBH	2012	https://doi.org/10.1136/thx.2009.129395
Case finding for COPD in primary care: a systematic review	<i>Primary Care Respiratory Journal</i>	Shamil M Haroon, Peymane A Adab, Rachel E Jordan	2012	https://doi.org/10.4104/pcrj.2012.00060

Conference proceedings

Title	Journal	Conference	Authors	Year	Volume	Issue	Pages
A Comparison Of The ADO, BODE And DOSE Scores For Predicting Respiratory Hospitalisations In A Primary Care COPD Cohort	<i>BMC Journal of Diagnostic & Prognostic Research</i>	MEMTAB	A Dickens, R Jordan, A Enocson, D Fitzmaurice, A Sitch, P Adab	2017	1 (Supp1):7. DOI: 10.1186/s41512-016-0001-y		
Screening Test Accuracy Of Case Finding Interventions For Chronic Obstructive Pulmonary Disease In Primary Care: A Systematic Review	<i>American Journal of Respiratory and Critical Care Medicine</i>	ATS 2014	Haroon SMM, Jordan RE, Adab P	2014	189		A2955
The Case Finding Yield For COPD In Primary Care: A Systematic Review And Meta-Analysis	<i>American Journal of Respiratory and Critical Care Medicine</i>	ATS 2014	Haroon SMM, Jordan RE, O'Bierne-Elliman J, Adab P	2014	189		A2955
Detecting COPD Among Symptomatic Patients In Primary Care: A Comparison Of The COPD Assessment Test And The COPD Diagnostic Questionnaire	<i>American Journal of Respiratory and Critical Care Medicine</i>	ATS 2014	Haroon SMM, Jordan RE, Enocson A, Fitzmaurice D, Adab P	2014	189		A2955
Over Diagnosis Of Chronic Obstructive Pulmonary Disease By GOLD Criteria Includes Older Male Subjects With Lower CAT Scores, More Heart Disease And Hypertension	<i>American Journal of Respiratory and Critical Care Medicine</i>	ATS 2014	Haroon SMM, Miller MR, Fitzmaurice DA, Enocson A, Jordan RE, Adab P	2014	189		A2955
Forced Vital Capacity Definition Substantially Alters Prevalence Of Chronic Obstructive Pulmonary Disease	<i>American Journal of Respiratory and Critical Care Medicine</i>	ATS 2014	Haroon SMM, Miller MR, Fitzmaurice DA, Enocson A, Jordan RE, Adab P	2014	189		A2955
Detecting undiagnosed COPD: Using routine primary care data to select and validate candidate variables for COPD risk prediction	<i>European Respiratory Journal</i>	ERS 2013	Haroon SMM, Jordan RE, Riley R, Lancashire R, Marshall T, Adab P	2013	42	Suppl. 57	2399

Conference presentations/posters

Date	Conference	Format	Title	Authors
2019	ERS	Oral presentation	Effect of screening for undiagnosed COPD on respiratory hospitalisation and mortality – 4-year follow-up of the TargetCOPD trial	Adab P, Fitzmaurice D, Martin J, Sitch A, Ayres JG, Cheng KK, Cooper BG, Daley A, Dickens AP, Enocson A, Greenfield S, Jolly K, Jowett S, Miller MR, Riley RD, Siebert S, Stockley RA, Turner A, Haroon S, Jordan RE
2019	ERS	Oral presentation	Development of the Birmingham Lung Improvement Studies (BLISS) prognostic score for COPD patients in primary care: data from the Birmingham COPD cohort	Jordan RE, Fitzmaurice D, Martin J, Sitch A, Ayres JG, Cheng KK, Cooper BG, Daley A, Dickens AP, Enocson A, Greenfield S, Jolly K, Jowett S, Miller MR, Riley RD, Siebert S, Stockley RA, Turner A, Haroon S, Adab P
2019	SAPC	Oral presentation	The impact of COPD case finding on clinical care: a prospective analysis of the TargetCOPD trial	Haroon S, Adab P, Dickens AP, Sitch A, Rai K, Enocson A, Fitzmaurice DA, Jordan RE
2019	RCGP Midland Faculty Research Symposium	Oral presentation	The impact of COPD case finding on clinical care: a prospective analysis of the TargetCOPD trial	Haroon S, Adab P, Dickens AP, Sitch A, Rai K, Enocson A, Fitzmaurice DA, Jordan RE
2019	ERS	Poster	External validation of the updated ADO score to predict mortality in patients from the Birmingham COPD cohort	Keene SJ, Jordan RE, de Vries F, Franssen FME, Martin J, Sitch A, Dickens A, Fitzmaurice DA, Adab P
2019	ERS	Oral presentation	Determinants of long-term changes in ADO prognostic score in UK COPD primary care patients: results from The Health Improvement Network	Keene
2019	ERS	Poster	The effects of COPD progression on work productivity: the Birmingham COPD Cohort	Kalirai R, Adab P, Ayres J, Fitzmaurice D, Jordan R on behalf of the BLISS investigators
2019	ERS	Oral presentation		Rai
2019	British Thoracic Society	Oral presentation	Three million needles in a haystack	R Jordan
2018	Society for Research on Nicotine & Tobacco Europe conference	Poster	Prevalence, views and experience of e-cigarette use by COPD patients in The Birmingham COPD Cohort	A Farley, M Swallow, R Jordan, A Enocson, A Dickens, D Kotz, D Fitzmaurice, P Adab
2018	ERS	Poster	Prevalence, views, and experience of e-cigarette use by COPD patients in the Birmingham COPD Cohort	M Swallow, A Farley, R Jordan, A Enocson, A Dickens, D Fitzmaurice, P Adab
2018	ERS	Poster	Clinical management of patients newly diagnosed with COPD through targeted case finding and routine care: A longitudinal analysis of the TargetCOPD trial	S Haroon, A Dickens, P Adab, A Sitch, K Rai, A Enocson, D Fitzmaurice, R Jordan
2017	ERS	Poster	Evaluating a simple lung monitor as a screening test for COPD in primary care	A Dickens, P Adab, D Fitzmaurice, B Cooper, M Miller, A Sitch, R Riley, A Enocson, R Jordan

Date	Conference	Format	Title	Authors
2017	SAPC	Elevator pitch presentation	Can a simple lung monitor be used as a screening test for COPD in primary care?	A Dickens, P Adab, D Fitzmaurice, B Cooper, M Miller, A Sitch, R Riley, A Enocson, R Jordan
2017	IPCRG World	Oral presentation	Evaluating a simple lung monitor as a screening test for COPD in primary care	R Jordan
2016	UHB Academic Grand Round	Invited speaker	Controversies in screening: the case of COPD	R Jordan
2016	IPCRG World	Oral presentation	Avoiding infections among patients with COPD: cross sectional analysis of the Birmingham COPD cohort	Jordan R, Woodall V, Sitch A, Khan A, Dickens A, Enocson A, Fitzmaurice D, Adab P
2016	COPD10	Poster	Prevalence and characteristics of low oxygen saturation (SpO ₂) in a primary care COPD cohort	A Enocson, RE Jordan, P Adab, AP Dickens, D Fitzmaurice
2016	COPD10	Poster	Delivering high quality spirometry in primary care: a report of spirometry quality in the BLISS programme	S Haroon, A Dickens, M Miller, B Cooper, A. Enocson, RE Jordan, D Fitzmaurice, P Adab
2016	COPD10	Poster	A Comparison Of The ADO, BODE And DOSE Scores For Predicting Respiratory Hospitalisations In A Primary Care COPD Cohort	A Dickens, R Jordan, A Enocson, D Fitzmaurice, A Sitch, P Adab
2016	COPD10	Poster	Prevalence Of Sleep Apnoea And Its Associated Impact On Quality Of Life In A Primary Care COPD Population	A Dickens, A Enocson, R Jordan, D Fitzmaurice, P Adab
2016	COPD10	Oral presentation	Early diagnosis of COPD. Insights from BLISS: The Birmingham Lung Improvement Studies	R Jordan
2016	COPD10	Oral presentation	Reflections on early identification of COPD	P Adab
2016	SAPC	Poster	A Comparison Of The ADO, BODE And DOSE Scores For Predicting Respiratory Hospitalisations In A Primary Care COPD Cohort	A Dickens, R Jordan, A Enocson, D Fitzmaurice, A Sitch, P Adab
2016	SAPC	Elevator pitch presentation	Prevalence of sleep apnoea and its associated impact on quality of life in a primary care COPD population	A Dickens, A Enocson, R Jordan, D Fitzmaurice, P Adab
2016	MEMTAB	Poster	A Comparison Of The ADO, BODE And DOSE Scores For Predicting Respiratory Hospitalisations In A Primary Care COPD Cohort	A Dickens, R Jordan, A Enocson, D Fitzmaurice, A Sitch, P Adab
2016	ERS	Poster	Prevalence and characteristics of low oxygen saturation (SpO ₂) in a primary care COPD cohort	A Enocson, RE Jordan, P Adab, AP Dickens, D Fitzmaurice
2016	ERS	Poster discussion	A Comparison Of The ADO, BODE And DOSE Scores For Predicting Respiratory Hospitalisations In A Primary Care COPD Cohort	A Dickens, R Jordan, A Enocson, D Fitzmaurice, A Sitch, P Adab

Date	Conference	Format	Title	Authors
2016	ERS	Poster	Prevalence Of Sleep Apnoea And Its Associated Impact On Quality Of Life In A Primary Care COPD Population	A Dickens, A Enocson, R Jordan, D Fitzmaurice, P Adab
2016	ERS	Poster	Predicting risk of undiagnosed COPD in primary care: Development and validation of the TargetCOPD score	S Haroon, P Adab, A Dickens, R Riley, D Fitzmaurice, R Jordan
2016	ERS	Poster	Prevalence and predictors of electronic cigarette use by patients with COPD in the Birmingham COPD cohort	A Farley, K Kalirai, R Jordan, A Enocson, A Dickens, D Fitzmaurice, P Adab
2016	ERS	Poster discussion	Modelling the long-term effects of an active case finding programme for undiagnosed COPD	T Lambe, R Jordan, P Adab, D Fitzmaurice, A Enocson, S Jowett
2016	ERS	Oral presentation	Using the ADO score in primary care to target pulmonary rehabilitation to patients at high risk of hospital admission: model using primary care cohorts and published literature	R Jordan, A Dickens, A Enocson, D Fitzmaurice, R Ryan, T Marshall, P Adab
2016	ERS	Invited speaker	What is the most clinically and cost-effective approach for identifying undiagnosed COPD?	R Jordan
2015	IPCRG World	Oral presentation	Predicting risk of undiagnosed COPD in primary care: Development and validation of the TargetCOPD model	S Haroon, R Jordan, R Riley, D Fitzmaurice, P Adab
2015	IPCRG World	Oral presentation	Case finding for COPD in primary care: a qualitative study of the views of health professionals	S Haroon, R Jordan, P Adab
2015	ATS	Poster	TargetCOPD: A pragmatic randomised controlled trial of targeted case finding for COPD versus routine practice in primary care	Jordan RE, Adab P, Sitch AJ, Enocson A, Blissett D, Jowett S, Riley RD, Marsh J, Miller MR, Cooper B, Turner AM, Ayres JG, Jolly K, Stockley R, Greenfield S, Siebert S, Daley A, Cheng KK, Fitzmaurice DA
2015	ERS	Oral presentation	COPD over diagnosis in the UK	Halima Buni, Rachel Jordan, Peymane Adab, Alexandra Enocson, Kar Keung Cheng
2015	ERS	Oral presentation	TargetCOPD: A pragmatic randomised controlled trial of targeted case finding for COPD versus routine practice in primary care	RE Jordan, P Adab, A Sitch, A Enocson, D Blissett, S Jowett, J Marsh, R Riley, M Miller, B Cooper, A Turner, JG Ayres, KK Cheng, K Jolly, R Stockley, S Greenfield, S Siebert, A Daley, D Fitzmaurice
2015	SAPC	Oral presentation	TargetCOPD: A cluster RCT of targeted case finding for COPD vs routine practice in primary care	Jordan RE, Adab P, Sitch AJ, Enocson A, Blissett D, Jowett S, Riley RD, Marsh J, Miller MR, Cooper B, Turner AM, Ayres JG, Jolly K, Stockley R, Greenfield S, Siebert S, Daley A, Cheng KK, Fitzmaurice DA
2014	ATS	Poster	Screening Test Accuracy Of Case Finding Interventions For Chronic Obstructive Pulmonary Disease In Primary Care: A Systematic Review	Haroon S, Jordan R, Adab P, Takwoingi Y

Date	Conference	Format	Title	Authors
2014	ATS	Poster	The Case Finding Yield For COPD In Primary Care: A Systematic Review And Meta-Analysis	Haroon S, Jordan R, Adab P, O'Beirne-Elliman J
2014	ATS	Poster	Over diagnosis of chronic obstructive pulmonary disease by GOLD criteria includes older male subjects with lower CAT scores, more heart disease and hypertension	Haroon S, Miller MR, Enocson A, Fitzmaurice DA, Jordan R, Adab P
2014	ATS	Poster	Forced vital capacity definition substantially alters prevalence of chronic obstructive pulmonary disease	Haroon S, Miller MR, Enocson A, Fitzmaurice DA, Jordan R, Adab P
2014	ATS	Poster	Detecting COPD among symptomatic patients in primary care: a comparison of the COPD Assessment Test and the COPD Diagnostic Questionnaire	Haroon S, Jordan R, Enocson A, Fitzmaurice D, and Adab P
2014	ATS	Poster	The Birmingham COPD Cohort Study: A Cross-sectional Comparison Of The Characteristics Of Ever-smokers And Never-smokers	Alexandra Enocson, Andy Dickens, Rachel Jordan, David Fitzmaurice, Peymane Adab
2014	IPCRG World	Oral presentation	The Birmingham COPD Cohort Study: A Cross-Sectional Comparison Of The Characteristics Of Ever-Smokers And Never-Smokers	R Jordan, A Enocson, A Dickens, D Fitzmaurice, P Adab
2014	IPCRG World	Oral presentation	Predicting the risk of COPD in Primary Care: Development and validation of a COPD risk score	S Haroon, R Riley, R Lancashire, T Marshall, R Jordan, P Adab
2014	IPCRG World	Invited speaker	Preventing COPD admissions: Strategies for risk prediction in Primary Care	R Jordan
2014	NIHR SPCR Primary Care Research Showcase	Poster	COPD Screener Study: Evaluation of a simple COPD screener as a novel screening test for case finding for COPD in primary care	Rachel Jordan, Nicola Adderley, Peymane Adab, Brendan Cooper, Alexandra Enocson, David Fitzmaurice, Martin Miller, Richard Riley
2014	ERS	Poster	Birmingham COPD Cohort: factors associated with absenteeism	Kiran Kalirai, Peymané Adab, Rachel Jordan, David Fitzmaurice, Jon Ayres
2014	Birmingham City Council in-house research meeting	Poster (not peer reviewed, MPH student)	The Birmingham COPD Cohort Study: A Cross-sectional Analysis of Self-Management Behaviours and Support in adults with COPD	Ainee Khan, Rachel Jordan, Andy Dickens, Alexandra Enocson, David Fitzmaurice, Peymane Adab
2014	ERS	Oral presentation	Comparison of characteristics of COPD patients with an established diagnosis, with those newly identified through case-finding – The Birmingham COPD Cohort Study	P Adab, A Dickens, A Enocson, D Fitzmaurice, R Jordan
2014	BTS	Poster	Feasibility of delivering an occupational health intervention aimed at improving work productivity among COPD working patients	K Kalirai, P Adab, RE Jordan, JG Ayres, S Sadhra

Date	Conference	Format	Title	Authors
2013	ERS	Poster	Detecting undiagnosed COPD: Using routine primary care data to select and validate candidate variables for COPD risk prediction	S Haroon, R Jordan, R Riley, R Lancashire, T Marshall, P Adab
2013	ERS	Poster	Birmingham COPD cohort: Comparison of characteristics of employed with non-employed patients	K Kalirai, P Adab, R Jordan, D Fitzmaurice, J Ayres
2013	ERS	Poster	The Birmingham COPD Cohort Study – Associations between CAT, lung health and health care utilisation	AP Dickens, P Adab, R Jordan, A Enocson, J Ayres, D Fitzmaurice
2013	RCGP symposium	Poster	Birmingham COPD Cohort: comparison of characteristics of employed with non-employed patients	K Kalirai, P Adab, R Jordan, D Fitzmaurice, J Ayres
2013	BTS	Oral presentation	A cross-sectional analysis of the effect of COPD on work capability using the Birmingham COPD cohort	K Kalirai, P Adab, R Jordan, D Fitzmaurice, J Ayres
2013	ERS	Poster	Birmingham COPD Cohort: comparison of characteristics of employed with non-employed patients	Kiran Kalirai; Peymane Adab; Rachel Jordan, David Fitzmaurice, Jon Ayres
2013	BTS	Poster	The relationship between employment status, work productivity and quality of life among patients with COPD: Cross-sectional analysis of the Birmingham COPD Cohort	K Kalirai, P Adab, R Jordan, D Fitzmaurice, J Ayres
2012	COPD8	Poster	The Birmingham COPD Cohort Study protocol: a primary care cohort of COPD patients	P Adab, A Dickens, R Backman, K Kalirai, A Enocson, D Fitzmaurice, J Ayres, KK Cheng, RE Jordan and the BLISS Investigators
2012	COPD8	Poster	TargetCOPD: a pragmatic randomised controlled trial of targeted case finding for COPD versus routine practice in primary care: protocol	Rachel Jordan, Ruth Backman, Andrew Dickens, David Fitzmaurice, Alexandra Enocson, Peymane Adab and the BLISS Investigators

ATS, American Thoracic Society; BTS, British Thoracic Society; ERS, European Respiratory Society; IPCRG, International Primary Care Respiratory Group; MEMTAB, Methods for Evaluating Medical Tests and Biomarkers; MPH, Masters of Public Health; NIHR SPCR, National Institute for Health Research School for Primary Care Research; RCGP, Royal College of General Practitioners; SAPC, Society for Academic Primary Care; UHB, University Hospitals Birmingham.

Appendix 2 Screening questionnaire for TargetCOPD trial



TargetCOPD QUESTIONNAIRE (GP Practice)

STUDY ID _____

Thank you for taking the time to fill in this questionnaire. Your input is very valuable so please complete as many questions as you are able and return to the receptionist.

Please try to answer every question with the closest answer possible by ticking the appropriate box.

SECTION 1: YOUR LUNG HEALTH

1. (a) Do you usually have a cough (either during the day, or night, or first thing in the morning)?

Yes

No (If No, go to Q2)

(b) Do you usually cough like this on most days for 3 consecutive months or more during the year?

Yes → If yes, for how many years have you had this cough?years

No

(c) Does the weather affect your cough? Yes No

2. (a) Do you ever cough up phlegm from your chest when you don't have a cold

Yes

No (If No, go to Q3)

(b) Do you usually bring up phlegm from your chest (either during the day, or night, or first thing in the morning)? Yes No

(c) Do you bring up phlegm on most days for 3 consecutive months or more during the year?

Yes → If yes, for how many years have you had trouble with phlegm?.....years

No

3. Have you had wheezing or whistling in the chest in the past 12 months?

Yes → If yes, how frequently do you wheeze?

Occasionally More often

No



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NHS
National Institute for
Health Research

4. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
Yes No
5. Do you get short of breath walking with other people of your own age on level ground or have to stop for breath after about 15 minutes when walking at your own pace?
Yes No
6. Do you have to stop for breath after walking about 100m or after a few minutes on level ground?
Yes No
7. Are you too breathless to leave the house, or breathless while dressing or undressing?
Yes No
8. Can you lie flat at night?
Yes
No → If no, how many pillows do you need **in total**?.....
9. Do you have or have you had any allergies?
Yes
No **(If No, go to Q11)**
10. If yes, what type of allergies? (tick any that apply)
Hay fever Eczema Skin allergies Allergic rhinitis (nose/eye symptoms)
Food allergies Other (please specify).....
11. Do you usually have a blocked or running nose? Yes No
12. Over the last year has your breathing kept you from doing as much as you used to?
Yes No

SECTION 2: YOUR GENERAL HEALTH AND CIRCUMSTANCES

13. How would you describe your health in general?
Very good Good Fair Bad Very bad
14. Has a doctor ever said you have (please tick any that apply):
- | | | | |
|--------------------|--------------------------|---------------------|--------------------------|
| Asthma | <input type="checkbox"/> | High blood pressure | <input type="checkbox"/> |
| COPD | <input type="checkbox"/> | Diabetes | <input type="checkbox"/> |
| Chronic bronchitis | <input type="checkbox"/> | Stroke | <input type="checkbox"/> |
| Emphysema | <input type="checkbox"/> | Lung cancer | <input type="checkbox"/> |
| Heart disease | <input type="checkbox"/> | Tuberculosis | <input type="checkbox"/> |



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Heart failure Depression
Other medical condition (please specify)

15. Have you ever had a paid job?

Yes Please state the occupation you have been employed in most of your life

.....
.....

Please describe what you do/did in this job

.....
.....
.....
.....

No

16. Have you ever worked in a job which exposed you to vapours, gas, dust or fumes?

Yes

No (If No, go to Q18)

17. If yes, for how many years have you been exposed?

18. (a) Have you ever smoked as much as one cigarette a day (or one cigar a week or an ounce of tobacco a month) for as long as one year? Yes

No (If No, go to Q19)

(b) (b) How much do/did you smoke a day?

.....cigarettes/daycigars/week.....oz org tobacco/week

(c) How old were you when you started smoking?.....

(d) Do you still smoke?

Yes (If Yes, go to Q19)

No

(e) How old were you when you finally stopped smoking?.....

19. In most weeks, how many hours per week are you exposed to other people's tobacco smoke?

20. What is your current height without shoes? metres **or**feet.....inches

21. What is your current weight without shoes?kg **or**.....stone.....pounds

22. Please indicate your date of birth:

23. Sex: Male Female



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24. How would you class your ethnic group? (Please tick one)

White

English/Welsh/Scottish/Northern

Irish/British Irish Gypsy/Irish Traveller Any other white background *Mixed / multiple ethnic groups*White & Black Caribbean White & Black African White & Asian Other mixed *Asian / Asian British*Indian Pakistani Bangladeshi Chinese Any other Asian background *Black / African / Caribbean / Black British*African Caribbean Any other Black / African / Caribbean
background *Other ethnic group*Arab Other Prefer not to say



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SECTION 3: CONTACT INFORMATION

25. Title..... First name.....

Surname

26. Address.....

.....
.....
.....

27. Postcode.....

28. Telephone number Home:.....

Mobile:.....

29. Email address.....

30. You may be invited for further assessment; to help us schedule these

appropriately please indicate your preferred appointment times (tick any when you are available)

Monday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>
Tuesday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>
Wednesday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>
Thursday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>
Friday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>
Saturday	morning	<input type="checkbox"/>	afternoon	<input type="checkbox"/>	evening	<input type="checkbox"/>

THANK YOU FOR TAKING THE TIME TO FILL OUT THIS QUESTIONNAIRE!

PLEASE LEAVE WITH THE RECEPTIONIST

Appendix 3 Baseline questionnaires for Birmingham chronic obstructive pulmonary disease cohort participants

The Birmingham COPD Cohort

Part of the Birmingham Lung Improvement

Studies (BLISS) programme



Baseline questionnaire

HOME COMPLETION BOOKLET

Your answers and opinions are valuable to us. We would be very grateful if you could read the below before turning the page:

- Please complete this questionnaire yourself if at all possible
- Please answer all questions as well as you can
- Do not spend too long thinking about your answers
- If someone is completing this on your behalf, they should record your answers

Patient Initials

Study ID

Date

In the following booklet we would like to ask you a few questions about yourself, your family and your home. Please take time to answer the questions (in blue or black ink) as best as you can and bring the completed booklet to your first assessment.

1.1 Sex

Male Female

1.2 Date of Birth

1.3 What is the highest level of qualification that you have?

- No formal qualification
- GCSE, CSE, O level or equivalent
- A-level/AS level or equivalent
- Degree level or higher
- Other (*Please specify*) _____

1.4 And which, if any, of the following vocational or professional qualifications have you obtained? Tick all that apply

- Level 1 NVQ or SVQ, Foundation GNVQ or GSVQ
- Level 2 NVQ or SVQ, Intermediate GNVQ or GSVQ
- Level 3 NVQ or SVQ, Advanced GNVQ or GSVQ
- Level 4 NVQ or SVQ
- Level 5 NVQ or SVQ
- Completion of trade apprenticeship
- Other vocational or pre-vocational qualifications, e.g. City and Guilds, RSA, OCR BTEC
- Other professional qualifications e.g. qualified teacher, accountant, nurse
- No vocational or professional qualifications

1.5 At what age did you complete your continuous full time education?

years

Never went to school

1.6 Do you live alone?

Yes No

1.7 What is your legal marital or same-sex civil partnership status?

Never married and never registered in a same-sex civil partnership

Married or in a registered same-sex civil partnership

Separated, but still legally married or in a same-sex civil partnership

Divorced or formerly in a same-sex civil partnership which is now legally dissolved

Widowed or surviving partner from a same-sex civil partnership

1.8 How many adults (Aged 16 years or over) live in the same household as you? (Apart from yourself - put zero if there are no other adults.)

1.9 How many dependents live with you? (Put zero if there are none.)

Children under 16 years

Other dependants

1.10 Do you regularly see relatives or friends? (Not counting those who live with you.)

Yes No *If no, please go to 1.12*

1.11 About how often do you see them?

Every day or nearly every day

Two or three times a week

Once a week

Once or twice a month

Less than one a month

1.12 How often are you able to confide in someone close to you?

- Almost daily
- 2-4 times per week
- About once per week
- About once per month
- Once every few months
- Never or almost never

2.1 Did you ever have bronchitis, pneumonia or severe whooping cough as a child?

Yes No ***If no, please go to 2.3***

2.2 If yes, approximately how old were you when you had this (or first time if several episodes)? years months

2.3 Do you know what your birth weight was?

Yes kg **OR** lb oz

No

2.4 Do you know if your birth weight was thought to be low, high or normal?

Low Normal High Don't know

2.5 Were you born prematurely?

Yes No Don't know

2.6 Have you ever had any nasal allergies including hayfever?

Yes No Don't know

2.7 Do you keep any household pets inside your house/flat?

Yes No ***If no, please go to 3.1***

2.8 If yes what pets do you keep inside?

Dog

Cat

Bird

Other furry pets

Other

3.1 Is your house...

Fully heated Part heated Not heated *please go to 3.4*

3.2 What is the main type of heating that you have in your current home?

Gas central heating

Electric central heating (including storage heaters)

Oil central heating

Solid fuel central heating (e.g. coal and wood)

Gas fires

Electric fires or radiators

Hot Air Heating

Other

3.3 How often do you use any of the following forms of heating in your home when it is cold?

	Never	Rarely	Sometimes	Always
Gas fire	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Electric heaters	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Closed solid fuel heater (stove)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Open fire/grate burning coal or wood	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3.4 During the winter months, does condensation form on the windows or walls of any room in your home, apart from bathroom, toilets and kitchen?

Yes No *If no, please go to 3.7*

3.5 Do you believe damp or condensation is a minor, moderate or serious problem in your home?

Minor Moderate Serious

3.6 Are there patches of mould or fungus in any room in your home, apart from bathroom, toilets or kitchen?

Yes No

3.7 Do you live on a main road or on a side street?

Main road Side street Other

3.8 How often do trucks pass through your residential street on a weekday?

- Never
- Seldom
- Frequently throughout the day
- Constantly

4.1 Do you have a nap during the daytime, especially after lunch?

- Yes
- No ***If no, please go to 4.4***

4.2 How often do you nap during the daytime?

- Daily
- Most days (4-6 days per week)
- Some days (1-3 days per week)
- <1 day per week

4.3 Approximately how long do your naps last on average?

minutes **or** hours

4.4 On average, how many hours of actual sleep do you normally get a day (over 24 hours)?

The following questions ask you about snoring. Feel free to check with anyone you live with if this will help you to better answer them.

4.5 Do you snore?

- Yes No Don't know ***If no or don't know, go to 4.9***

4.6 Is your snoring?

- Slightly louder than breathing
- As loud as talking
- Louder than talking
- Very loud...can be heard in adjacent rooms

4.7 How often do you snore?

- Almost every day
- 3-4 times a week
- 1-2 times a week
- 1-2 times a month
- Rarely or never

4.8 Has your snoring ever bothered other people?

Yes No

4.9 Has anyone noticed that you stop breathing for a short while during your sleep?

- Almost every day
- 3-4 times a week
- 1-2 times a week
- 1-2 times a month
- Rarely or never

4.10 How often do you feel tired or fatigued after your sleep?

- Almost every day
- 3-4 times a week
- 1-2 times a week
- 1-2 times a month
- Rarely or never

4.11 During your waking time, do you feel tired, fatigued or not up to par?

- Almost every day
- 3-4 times a week
- 1-2 times a week
- 1-2 times a month
- Rarely or never

4.12 Have you ever nodded off or fallen asleep while driving a vehicle?

Yes No

4.13 If yes, how often does it occur?

- Almost every day
- 3-4 times a week
- 1-2 times a week
- 1-2 times a month
- Rarely or never

5.1 How are your lung problems? For each item below place a mark in the box that best describes your experience on a scale of 0-5.

Example: I am very happy

0	√	1	2	3	4	5
---	---	---	---	---	---	---

 I am very sad

I never cough	0	1	2	3	4	5	I cough all the time
I have no phlegm (mucus) in my chest at all	0	1	2	3	4	5	My chest is completely full of phlegm
My chest does not feel tight at all	0	1	2	3	4	5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0	1	2	3	4	5	When I walk up a hill or one flight of stairs I am breathless
I am not limited doing any activities at home	0	1	2	3	4	5	I am very limited doing activities at home
I am confident leaving home despite my lung condition	0	1	2	3	4	5	I am not confident leaving my home because of my lung condition
I sleep soundly	0	1	2	3	4	5	I don't sleep soundly because of my lung condition
I have lots of energy	0	1	2	3	4	5	I have no energy at all

6.1 Do you regularly take any of the following medications? (*Tick all that apply*)

- Cholesterol lowering medication
- Blood pressure medication
- Insulin
- Arthritis medication
- Hormone replacement therapy (women only)
- None of the above

6.2 Do you regularly take any of the following medications for your lung problems? (*Tick all that apply*)

- Beta-2 agonist (BLUE inhaler)
- Inhaled steroid (BROWN or RED inhaler)
- Atrovent/Spiriva (GREY inhaler)
- Seretide (PURPLE inhaler)
- Symbicort (WHITE AND RED inhaler)
- Uniphylline/aminophylline tablets
- Steroid tablets
- Oxygen
- Other ***Please specify*** _____
- None of the above

6.3 Do you regularly take any other PRESCRIPTION medications? (Do not forget medications such as puffers, patches or eye drops.)

Yes No

6.4 Do you regularly take any of the following NON-PRESCRIPTION medications? (Tick all that apply)

- | | |
|------------------------------------|----|
| Aspirin | == |
| Ibuprofen (e.g. Nurofen) | == |
| Paracetamol | == |
| Ranitidine (e.g. Zantac) | == |
| Omeprazole (e.g. Zanprol) | == |
| Laxatives (e.g. dulcolax, senokot) | == |
| None of the above | == |

6.5 Do you regularly take any of the following? (Tick all that apply)

- | | |
|-------------------------------|----|
| Vitamin A | == |
| Vitamin B | == |
| Vitamin C | == |
| Vitamin D | == |
| Vitamin E | == |
| Folic acid or Folate (Vit B9) | == |
| Multivitamins +/- minerals | == |
| None of the above | == |

6.6 Do you regularly take any of the following? (Tick all that apply)

- | | |
|------------------------------------|----|
| Fish oil (including cod liver oil) | == |
| Glucosamine | == |
| Calcium | == |
| Zinc | == |
| Iron | == |
| Selenium | == |
| None of the above | == |

7.1 What is your ethnic group?

Choose one section from A to E, then tick one box to best describe your ethnic group or background

A White

- English/Welsh/Scottish/Northern Irish/British
- Irish
- Any other White background, write in _____

B Mixed/multiple ethnic groups

- White and Black Caribbean
- White and Black African
- White and Asian
- Any other Mixed/multiple ethnic backgrounds, write in _____

C Asian/Asian British

- Indian
- Pakistani
- Bangladeshi
- Chinese
- Any other Asian background, write in _____

D Black/African/Caribbean/Black British

- African
- Caribbean
- Any other Black/African/Caribbean background, write in _____

E Other ethnic group

- Arab
- Any other ethnic group, write in _____

- Prefer not to say**

7.2 In which country were you born? (Tick one box only)

England

Wales

Scotland

Northern Ireland

Republic of Ireland

Elsewhere (Please specify)

7.3 What is your religion?

No religion

Christian

Buddhist

Hindu

Jewish

Muslim

Sikh

Any other religion (Please specify)

Prefer not to say

8. Please list all the jobs you have ever had in the space below
Please include as many jobs as you can remember, starting with your first job since school and including any periods of unemployment and retirement.

Date Started	Date finished	Job title	Full time (FT)/part time (PT)	Main duties	Reason left

Finally, please tick one of the below boxes

- I completed this questionnaire myself
- Someone else has completed this questionnaire on my behalf

**Thank you for taking the time to complete this
survey**

The Birmingham COPD Cohort
Part of the Birmingham Lung Improvement
StudieS (BLISS) programme



Baseline questionnaire
LIFESTYLE BOOKLET

Your answers and opinions are valuable to us. We would be very grateful if you could read the below before turning the page:

- Please complete this questionnaire yourself if at all possible
- Please answer all questions as well as you can
- Do not spend too long thinking about your answers
- If someone is completing this on your behalf, they should record your answers

Patient Initials

Study ID

Date

In the following booklet we would like to ask you a few questions about your lifestyle. Please take time to answer the questions as accurately as possible.

1. Smoking

L.1.1 Have you ever smoked a cigarette, cigar or pipe regularly? (by regularly we mean at least 1 cigarette/day or 7 cigarettes/ week for at least 6 months)

- No, never smoked = **If no, please go to L.1.9**
- No, smoked occasionally, but never regularly =
- Yes, I used to, or still smoke regularly =

L.1.2 How old were you when you first tried smoking, even if it was only a puff or two?

	Write in how old you were then
--	--------------------------------

L.1.3 How much do you usually smoke each day now, or did you smoke before giving up? (if less than one a day, please write 0)

Filter cigarettes		number/day
Non-filter/hand rolled cigarettes		number/day
Cigars		number/day
Pipe tobacco		= oz/day or = g/day tobacco

L.1.4 Do you still smoke now?

- Yes = No, I have stopped smoking = **If no, please go to L.1.8**

L.1.5 Would you like to give up smoking altogether?Yes No **L.1.6 Have you ever tried to give up smoking?**Yes No **If no, please go to L1.9****L.1.7 How many times have you tried to give up smoking?**

number of quit attempts

L.1.8 How long ago did you last stop smoking daily?

years (if less than one please write 0)

L.1.9 Did your father ever smoke regularly when you were a child?*Please tick one box only*Yes No Don't know **L.1.10 Did your mother ever smoke regularly when you were a child?***Please tick one box only*Yes No Don't know **L1.11 Did anyone else in your house ever smoke regularly when you were a child? Please tick one box only**Yes No Don't know

If yes, who? _____

L.1.12 Do you find that you are often near people who are smoking in any of the following places? Please tick all the places where you are often near people who are smoking

At home	<input type="checkbox"/>	At work	<input type="checkbox"/>
In other people's homes	<input type="checkbox"/>	In other places	<input type="checkbox"/>
No, none of these	<input type="checkbox"/>	please go to L1.14	

L.1.13 In most weeks now, how many hours a week are you exposed to other people's tobacco smoke at home, at work, and in other places?

L1.13.1	<input type="text"/>	Number of hours a week at home
L1.13.2	<input type="text"/>	Number of hours a week at work
L1.13.3	<input type="text"/>	Number of hours a week in other places

L.1.14 In the past, in your adult life (before the 2007 smoking ban) did you find that you were often near people who were smoking in any of these places? *Please tick all the places where you were often near people who were smoking*

- | | | | |
|-------------------------|--------------------------|---------------------------|--------------------------|
| At home | <input type="checkbox"/> | At work | <input type="checkbox"/> |
| In other people's homes | <input type="checkbox"/> | In other places | <input type="checkbox"/> |
| No, none of these | <input type="checkbox"/> | please go to L1.16 | |

L.1.15 In the past, in your adult life (before the 2007 smoking ban) how many hours a week were you exposed to other people's tobacco smoke at home, at work, and in other places?

- | | | |
|----------|----------------------|----------------------------------------|
| L.1.15.1 | <input type="text"/> | Number of hours a week at home |
| L.1.15.2 | <input type="text"/> | Number of hours a week at work |
| L.1.15.3 | <input type="text"/> | Number of hours a week in other places |

L.1.16 Have you ever smoked cannabis (marijuana, dope, hash, blow, joints)?

Yes No **If no, please go to L1.18**

L.1.17 How often do you smoke cannabis now?

- | | |
|-----------------------|--------------------------|
| Never | <input type="checkbox"/> |
| A few times a year | <input type="checkbox"/> |
| Once or twice a month | <input type="checkbox"/> |
| At least once a week | <input type="checkbox"/> |
| Most days | <input type="checkbox"/> |

L.1.18 Have you ever smoked a shisha pipe (hookah, waterpipe)?

Yes No **If no, please go to section 2**

L.1.19 How often do you smoke shisha pipes now?

- | | |
|-----------------------|--------------------------|
| Never | <input type="checkbox"/> |
| A few times a year | <input type="checkbox"/> |
| Once or twice a month | <input type="checkbox"/> |
| At least once a week | <input type="checkbox"/> |
| Most days | <input type="checkbox"/> |

2. Alcohol Intake

L.2.1 During the past 12 months, have you consumed at least one alcoholic drink of any kind? This includes beer, wine, spirits or any drink containing alcohol.

Yes = ***If yes go to L.2.3*** No = ***If no, go to L.2.2***

L.2.2 Have you ever consumed at least one alcoholic drink of any kind?

No (=never drink) = ***If no, please go to L3.1***

Yes – but less than once per year = ***please go to L3.1***

Yes, used to drink at least once per week (former drinker) = ***When did you stop drinking?***
(If less than one year use 0)
 years ago

L.2.3 During the past 12 months, or when you used to drink, about how often did you drink alcohol?

Daily or almost every day = Once every couple of months =

Three or four times a week = Only on special occasions (once or twice per year) =

1-3 times a month =

L.2.4 During the past 12 months, or when you used to drink, how much and what type of alcohol would you usually consume per week?

L2.4.1 In an average WEEK, how many glasses of wine or champagne would you drink? (There are six glasses in an average bottle)

L2.4.2 In an average WEEK how many pints of beer or cider would you drink? (Include bitter, lager, stout, ale, Guinness)

L2.4.3 In an average WEEK how many measures of spirits or liqueurs would you drink? (There are 25 standard measures in a normal sized bottle; spirits include drinks such as whisky, gin, rum, vodka, brandy)

L2.4.4 In an average WEEK how many glasses of fortified wine (e.g. sherry, vermouth, port) would you drink? (There are 12 glasses in an average bottle)

L2.4.5 In an average WEEK how many glasses of other alcoholic drinks (such as alcopops) would you drink?

L.2.5 During what period of your life did you drink alcohol most? (tick one box)

Less than 20yrs 20-29yrs 30-39yrs 40-49yrs 50-59yrs
 60yrs+

L.2.6 How much did you drink at that time?

Same as above — **Please go to section 3**

If different from above, please answer the following questions:

L2.6.1 In an average WEEK, how many glasses of wine or champagne would you drink? (There are six glasses in an average bottle)

L2.6.2 In an average WEEK how many pints of beer or cider would you drink? (Include bitter, lager, stout, ale, Guinness)

L2.6.3 In an average WEEK how many measures of spirits or liqueurs would you drink? (There are 25 standard measures in a normal sized bottle; spirits include drinks such as whisky, gin, rum, vodka, brandy)

L2.6.4 In an average WEEK how many glasses of fortified wine (e.g. sherry, vermouth, port) would you drink? (There are 12 glasses in an average bottle)

L2.6.5 In an average WEEK how many glasses of other alcoholic drinks (such as alcopops) would you drink?

3. Physical activity

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and gardening work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**.

Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Think *only* about those physical activities that you did for at least 10 minutes at a time.**

L3.1 During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?

Days per week

— No vigorous physical activities (*please go to L3.3*)

L3.2 How much time did you usually spend doing vigorous physical activities on one of those days?

hours per day minutes per day — Don't know/not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

L3.3 During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

days per week = No moderate physical activities (*please go to L3.5*)

L3.4 How much time did you usually spend doing moderate physical activities on one of those days?

hours per day minutes per day = Don't know/not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

L3.5 During the last 7 days, on how many days did you walk for at least 10 minutes at a time?

days per week = No walking, *please go to question L3.7*

L3.6 How much time did you usually spend walking on one of those days?

hours per day minutes per day = Don't know/not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

L3.7 During the last 7 days, how much time did you spend sitting on a week day?

hours per day minutes per day = Don't know/not sure

L.3.8 In a typical day in summer, how many hours do you spend outdoors?

hours = Less than one hour per day

L.3.9 In a typical day in winter, how many hours do you spend outdoors?

hours = Less than one hour per day

4. Your diet

L.4.1 On average how many heaped tablespoons of COOKED vegetables would you eat per DAY? (do not include potatoes; put "0" if you do not eat any)

tablespoons Less than one Don't know

L.4.2 On average how many heaped tablespoons of SALAD or RAW vegetables would you eat per DAY? (include lettuce, tomato in sandwiches; put "0" if you do not eat any)

tablespoons Less than one Don't know

L.4.3 About how many pieces of FRESH fruit would you eat per DAY? (Count one apple, one banana, 10 grapes etc as one piece; put "0" if you do not eat any)

pieces Less than one Don't know

L.4.4 About how many pieces of DRIED fruit would you eat per DAY? (Count one prune, one dried apricot, 10 raisins etc as one piece; put "0" if you do not eat any)

pieces Less than one Don't know

L.4.5 How often do you eat oily fish? (eg: sardines, salmon, mackerel, herring)

Never Less than once a week Once a week
 2-4 times a week 5-6 times a week Once or more daily

L.4.6 How often do you eat other types of fish? (eg: cod, tinned tuna, haddock)

Never Less than once a week Once a week
 2-4 times a week 5-6 times a week Once or more daily

L.4.7.1 Do you eat meat?

Yes *if yes, please go to L4.8* No

L4.7.2 How old were you when you last ate any kind of meat? (Enter "0" if you have never eaten meat in your lifetime) years

L.4.8 Which of the following do you NEVER eat? (you can select more than one answer)

- Eggs or foods containing eggs
- Dairy products
- Wheat products
- Sugar or foods/drinks containing sugar
- I eat all of the above

L.4.9 How often do you eat cheese (include cheese in pizzas, quiches, cheese sauce)? Select one from

- Never Less than once a week
- Once a week 2-4 times a week
- 5-6 times a week Once or more daily

L.5.1 What type of milk do you mainly use? *Select one from*

- Full cream
- Semi-skimmed
- Skimmed
- Soya
- Other type of milk Please specify _____
- Never/rarely have milk

**L.5.2 Do you add salt to your food? (do not include salt used in cooking)
*Select one from***

- Never/rarely
- Sometimes
- Usually
- Always

L.5.3 How many cups of green tea do you drink each DAY?

cups less than one none

L.5.4 How many cups of black tea (with or without milk do you drink each DAY?

cups less than one none

L.5.5 How many cups of other tea do you drink each DAY?

cups less than one none

L.5.6 How many cups of coffee do you drink each DAY? (include decaffeinated coffee)

cups less than one none

L.5.7 What type of coffee do you usually drink? *Select one from*

- Decaffeinated coffee (any type)
- Instant coffee
- Ground coffee (include espresso, filter etc)
- Other type of coffee *Please specify* _____

L.5.8 How many glasses of water do you drink each DAY?

glasses less than one none

L.5.9 Have you made major changes to your diet in the last 5 years? *Select one from*

- No
- Yes, because of illness
- Yes, because of other reasons *Please specify* _____

Finally, please tick one of the below boxes

- I completed this questionnaire myself
- Someone else has completed this questionnaire on my behalf

Thank you for taking the time to complete this survey

The Birmingham COPD Cohort

**Part of the Birmingham Lung Improvement
StudieS (BLISS) programme**



Baseline questionnaire

YOUR HEALTH

Your answers and opinions are valuable to us. We would be very grateful if you could read the below before turning the page:

- Please complete this questionnaire yourself if at all possible
- Please answer all questions as well as you can
- Do not spend too long thinking about your answers
- If someone is completing this on your behalf, they should record your answers

Patient Initials

Study ID

Date

We would like to find out some more detail about your general health and medical history. Please take a few minutes to fill out this section.

H.1 How is your health in general?

Very Good Good Fair Bad Very Bad

H.2 Medical conditions

Has a doctor EVER told you that you had any of the following conditions?

Please tick all that apply

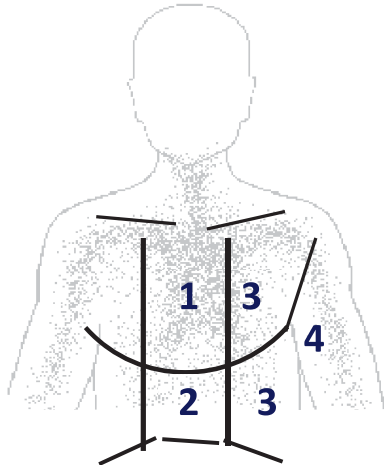
	Yes	No	
Cancer (Please state type)	<input type="checkbox"/>	<input type="checkbox"/>	_____
Diabetes	<input type="checkbox"/>	<input type="checkbox"/>	
High blood pressure	<input type="checkbox"/>	<input type="checkbox"/>	
Coronary heart disease/Angina/Heart Attack	<input type="checkbox"/>	<input type="checkbox"/>	
Heart failure	<input type="checkbox"/>	<input type="checkbox"/>	
Any other heart problem (Please specify)	<input type="checkbox"/>	<input type="checkbox"/>	_____
Stroke/mini-stroke	<input type="checkbox"/>	<input type="checkbox"/>	
Chronic Obstructive Pulmonary Disorder/chronic bronchitis/emphysema	<input type="checkbox"/>	<input type="checkbox"/>	
Asthma	<input type="checkbox"/>	<input type="checkbox"/>	
Tuberculosis	<input type="checkbox"/>	<input type="checkbox"/>	
Cataract	<input type="checkbox"/>	<input type="checkbox"/>	
Osteoarthritis	<input type="checkbox"/>	<input type="checkbox"/>	
Rheumatoid arthritis	<input type="checkbox"/>	<input type="checkbox"/>	
Osteoporosis	<input type="checkbox"/>	<input type="checkbox"/>	
Depression	<input type="checkbox"/>	<input type="checkbox"/>	
Hay fever	<input type="checkbox"/>	<input type="checkbox"/>	
Eczema	<input type="checkbox"/>	<input type="checkbox"/>	
Skin allergies	<input type="checkbox"/>	<input type="checkbox"/>	
Other condition (Please specify)	<input type="checkbox"/>	<input type="checkbox"/>	_____

H.3 Chest symptoms

Question 1 Do you ever have any pain or discomfort in your chest?

Yes No (If no, please go to section H.4)

Question 2 Where do you get this pain or discomfort? (*Mark on the appropriate places on the chest below*)



1. Sternum (upper or middle)
2. Sternum (lower)
3. Left anterior chest
4. Left arm
5. Other

Question 3 When you walk at an ordinary pace on the level, does this produce the pain?

Yes No

Question 4 When you walk uphill or hurry, does this produce the pain?

Yes No

Question 5 When you get any pain or discomfort in your chest on walking, what do you do?

Stop Slow down Continue at the same pace

Question 6 Does the pain or discomfort in your chest go away if you stand still?

Yes No

Question 7 How long does it take to go away?

10 minutes or less More than 10 minutes

Question 8 Have you ever had a severe pain across the front of your chest lasting for half an hour or more?

Yes No (If no, please go to section H.4)

Question 9 If YES did you see a doctor because of this pain?

Yes No (If no, please go to question 11)

Question 10 If YES, what did they say it was?

- | | | | |
|------------------------|--------------------------|----------------------|--------------------------|
| Angina | <input type="checkbox"/> | Bone & muscle | <input type="checkbox"/> |
| Myocardial infarction | <input type="checkbox"/> | Mental/psychological | <input type="checkbox"/> |
| Coronary heart disease | <input type="checkbox"/> | Do not know | <input type="checkbox"/> |
| Respiratory disease | <input type="checkbox"/> | | |

Question 11 How many of these attacks have you ever had?

episodes

H.4 Fractures

Question 1 Since you were 40 years old has a doctor EVER told you that you had a fracture?

Yes No

Question 2 How many fractures have you had?

fractures

Question 3 Which sites were affected by a fracture and in approximately which year?

- | | | |
|--------------------------|-----------------|-------------|
| <input type="checkbox"/> | Femur | Year: _____ |
| <input type="checkbox"/> | Pelvis | Year: _____ |
| <input type="checkbox"/> | Tibia or fibula | Year: _____ |
| <input type="checkbox"/> | Foot or ankle | Year: _____ |
| <input type="checkbox"/> | Hand or wrist | Year: _____ |
| <input type="checkbox"/> | Forearm | Year: _____ |
| <input type="checkbox"/> | Humerus | Year: _____ |
| <input type="checkbox"/> | Ribs | Year: _____ |
| <input type="checkbox"/> | Skull or face | Year: _____ |
| <input type="checkbox"/> | Vertebrae | Year: _____ |
| <input type="checkbox"/> | Other | Year: _____ |

H.5 Stomach complaints

Question 1 Has a doctor EVER told you that you have a peptic (gastric or stomach) ulcer?

Yes No



If yes, approximately what year was this diagnosis made? _____

Question 2 Has a doctor EVER told you that you have dyspepsia or indigestion?

Yes No

If yes, approximately what year was this diagnosis made? _____

Question 3

Please answer both parts of each question		A	B
		often have you <i>had</i> this symptom the last 2 months? <small>only one box per question.</small>	How often <i>has</i> this symptom interfered with your normal activities (eating, sleeping, work, leisure) over the last 2 months? <small>Tick only one box per question</small>
1. Indigestion Indigestion is a pain or discomfort in the upper abdomen. 	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	
2. Heartburn Heartburn is a burning feeling behind the breastbone. 	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	
3. Regurgitation Regurgitation is an acid taste coming up into your mouth from your stomach.	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	
4. Nausea Nausea is a feeling of sickness without actually being sick.	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	<input type="checkbox"/> Not at all <input type="checkbox"/> Less than once a month <input type="checkbox"/> Between once a month and once a week <input type="checkbox"/> Between once a week and once a day <input type="checkbox"/> Once a day or more	
5. Which, if any, of these symptoms has been the most troublesome to you in the last 2 months? Please tick one box only		<input type="checkbox"/> Heartburn <input type="checkbox"/> Regurgitation <input type="checkbox"/> Indigestion <input type="checkbox"/> Nausea <input type="checkbox"/> None of these have troubled me	

H.6 Oral Health

Question 1 Excluding your four wisdom teeth, do you have your own natural teeth? (adults usually have 28 teeth excluding their wisdom teeth)

- No, only dentures
- Yes all
- Yes, but lost _____ teeth

Question 2 How often do you clean your teeth/dentures nowadays?

- More than twice per day
- Twice per day
- Once per day
- Less than once per day
- Rarely/never

Question 3 How often do your gums bleed when you brush?

- Always
- Sometimes
- Occasionally
- Rarely/never

Question 4 Do you have any fillings?

- Yes I have _____ fillings
- No

H.7 Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about

I have slight problems in walking about

I have moderate problems in walking about

I have severe problems in walking about

I am unable to walk about

SELF-CARE

I have no problems washing or dressing myself

I have slight problems washing or dressing myself

I have moderate problems washing or dressing myself

I have severe problems washing or dressing myself

I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems doing my usual activities

I have slight problems doing my usual activities

I have moderate problems doing my usual activities

I have severe problems doing my usual activities

I am unable to do my usual activities

PAIN / DISCOMFORT

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extreme pain or discomfort

ANXIETY / DEPRESSION

I am not anxious or depressed

I am slightly anxious or depressed

I am moderately anxious or depressed

I am severely anxious or depressed

I am extremely anxious or depressed

H.8 Respiratory Symptoms

Question 1 Do you usually cough first thing (upon waking) in the morning?

Yes No

Question 2 Do you usually cough either during the day or night?

Yes No

If yes for either of these questions please go to next question, otherwise go to question 9

Question 3 Do you cough like this on most days for as much as three consecutive months each year?

Yes No

Question 4 For how many years have you had this cough?

years

Question 5 Do you usually bring up any phlegm from your chest first thing (upon waking) in the morning?

Yes No

Question 6 Do you usually bring up any phlegm from your chest either during the day or at night?

Yes No

If yes for either question 5 or question 6 go to the next question, otherwise go to question 9

Question 7 Do you bring up phlegm like this on most days for as much as three months each year?

Yes No

Question 8 For how many years have you had this trouble with phlegm?

years

Question 9 In the past three years, have you had a period of increased cough and phlegm lasting three weeks or more?

Yes No

If yes go to the next question, otherwise go to question 11

Question 10 What is the total number of such periods, lasting three weeks or more in the last three years?

Episodes

Question 11 Are you troubled by shortness of breath when hurrying on the level ground or walking up a slight hill?

Yes No

Question 12 Do you get short of breath walking with other people of your own age on level ground?

Yes No

Question 13 Do you have to stop for breath when walking at your own pace on level ground?

Yes No

Question 14 Do you have to stop for breath after walking for 100yds (or after a few minutes) on the level?

Yes No

Question 15 Are you too breathless to leave the house or are you breathless when dressing or undressing?

Yes No

Question 16 Does your chest ever sound wheezing or whistling?

Yes No

Question 17 Do you get this on most days or nights?

Yes No

Question 18 Have you ever had attacks of shortness of breath with wheezing?

Yes No

Question 19 Do you usually have a blocked or running nose?

Yes No

H.9 St. George's Respiratory Questionnaire (SGRQ-C)

This part of the questionnaire is designed to help us learn much more about how your breathing is troubling you and how it affects your life. We are using it to find out which aspects of your illness cause you most problems, rather than what the doctors and nurses think your problems are. Please read the instructions carefully and ask if you do not understand anything. Do not spend too long deciding about your answers.

PART 1

Questions about how much chest trouble you have.

Please tick **ONE** box for each question:

Question 1. I cough:

- most days a week
- several days a week
- only with chest infections
- not at all

Question 2. I bring up phlegm (sputum):

- most days a week
- several days a week
- only with chest infections
- not at all

Question 3. I have shortness of breath:

- most days a week
- several days a week
- not at all

Question 4. I have attacks of wheezing

- most days a week
- several days a week
- a few days a month
- only with chest infections
- not at all

Question 5. How many attacks of chest trouble did you have during the last year?

- 3 or more attacks
- 1 or 2 attacks
- None

Question 6. How often do you have good days (with little chest trouble)?

- No good days
- a few good days
- most days are good
- every day is good

Question 7. If you have a wheeze, is it worse in the morning?

- No
- Yes

PART 2

Question 8. How would you describe your chest condition? Please tick **ONE**:

- Causes me a lot of problems or is the most important problem I have
- Causes me a few problems
- Causes no problem

Question 9. Questions about what activities usually make you feel breathless For each statement please tick in the box that applies to you **these days**:

	True	False
Getting washed or dressed	<input type="checkbox"/>	<input type="checkbox"/>
Walking around the home	<input type="checkbox"/>	<input type="checkbox"/>
Walking outside on the level	<input type="checkbox"/>	<input type="checkbox"/>
Walking up a flight of stairs	<input type="checkbox"/>	<input type="checkbox"/>
Walking up hills	<input type="checkbox"/>	<input type="checkbox"/>

Question 10. Some more questions about your cough and breathlessness

For each statement please tick in the box that applies to you **these days**:

	True	False
My cough hurts	<input type="checkbox"/>	<input type="checkbox"/>
My cough makes me tired	<input type="checkbox"/>	<input type="checkbox"/>
I am breathless when I talk	<input type="checkbox"/>	<input type="checkbox"/>
I am breathless when I bend over	<input type="checkbox"/>	<input type="checkbox"/>
My cough or breathing disturbs my sleep	<input type="checkbox"/>	<input type="checkbox"/>
I get exhausted easily	<input type="checkbox"/>	<input type="checkbox"/>

Question 11. These are questions about other effects that your chest trouble may have on you.

For each statement please tick in *the box* that applies to you **these days**:

	True	False
My cough or breathing is embarrassing in public	==	==
My chest trouble is a nuisance to my family, friends or neighbours	==	==
I get afraid or panic when I cannot get my breath	==	==
I feel that I am not in control of my chest problem	==	==
I have become frail or an invalid because of my chest	==	==
Exercise is not safe for me	==	==
Everything seems too much of an effort	==	==

Question 12. These are questions about how your activities might be affected by your breathing.

For each statement please tick in *the box* that applies to you **because of your breathing**:

	True	False
I take a long time to get washed or dressed	==	==
I cannot take a bath or shower, or I take a long time	==	==
I walk slower than other people, or I stop for rests	==	==
Jobs such as housework take a long time, or I have to stop for rests	==	==
If I walk up one flight of stairs, I have to go slowly or stop	==	==
If I hurry or walk fast, I have to stop or slow down	==	==
My breathing makes it difficult to do things such as walk up hills, carrying things up stairs, light gardening such as weeding, dance, play bowls or play golf	==	==
My breathing makes it difficult to do things such as carry heavy loads, dig the garden or shovel snow, jog or walk at 5 miles per hour, play tennis or swim	==	==

Question 13. We would like to know how your chest trouble usually affects your daily life.

For each statement please tick in *the box* that applies to you **because of your breathing**:

	True	False
I cannot play sports or games	=	=
I cannot go out for entertainment or recreation	=	=
I cannot go out of the house to do the shopping	=	=
I cannot do housework	=	=
I cannot move far from my bed or chair	=	=

Question 14. How does your chest trouble affect you?

Please tick **ONE**:

It does not stop me doing anything I would like to do	=
It stops me doing one or two things I would like to do	=
It stops me doing most of the things I would like to do	=
It stops me doing everything I would like to do	=

H.10 Over the past 12 months have you had any of the following major events in your life?

	Yes	No
Marital separation/divorce	==	==
Loss of job/retirement	==	==
Business bankrupt	==	==
Violence	==	==
Major conflict within family	==	==
Major injury or traffic accident	==	==
Death of spouse	==	==
Death/major illness of other close family member	==	==
Major natural disaster (e.g. flood & drought)	==	==
Loss of income/living in debt	==	==

H.11 In the past two weeks, have you been bothered by:

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	==	==	==	==
2. Feeling down, depressed or hopeless	==	==	==	==

H.12 In the last 12 months have you had one or more courses of oral steroids (prednisolone) for your lung problems?

- Yes, one course
- Yes, 2 courses
- Yes, more than 2 courses
- No
- Don't know

H.13 In the last 12 months have you had one or more courses of antibiotics for your lung problems?

- Yes, one course
- Yes, 2 courses
- Yes, more than 2 courses
- No
- Don't know

H.14 Have you ever been offered pulmonary rehabilitation?

- Yes No Don't know ***If no or don't know, please go to H.17***

H.15 If yes, have you ever attended pulmonary rehabilitation?

- Yes No

H.16 If yes, when did you last attend pulmonary rehabilitation?

- In the last 12 months
- 1-2 years ago
- > 2 years ago

H.17 Have you been given written advice on what to do if your symptoms get worse?

- Yes
- No
- Don't know

H.18 How many times have you consulted the following health care personnel regarding your health during the past 14 days?

GP	<input type="text"/>	times
Practice nurse	<input type="text"/>	times
Pharmacist	<input type="text"/>	times
None	Please go to H.20	

H.19 If you have consulted someone in the last 14 days, please select reasons for your consultation(s) and specify the number of times this applied

		Number of times
Respiratory (lung) disease	=	<input type="text"/>
Diabetes	=	<input type="text"/>
Accident/Injury	=	<input type="text"/>
Gastro-Intestinal problem (stomach/ intestines)	=	<input type="text"/>
Neurological	=	<input type="text"/>
Muscle/joint/arthritis	=	<input type="text"/>
Heart disease	=	<input type="text"/>
Headache	=	<input type="text"/>
Mental/psychological	=	<input type="text"/>
Other	=	<input type="text"/>

H.20 In the last 12 months have you been admitted to hospital (spent at least one night) for your lung problems?

Yes No If no, please go to question

Admission	No. of nights
1st	<input type="text"/>
2nd	<input type="text"/>
3rd	<input type="text"/>
Total	<input type="text"/>

H.21 If yes, how many times? (please use table provided to help you)

<input type="text"/>	admissions in last 6 months
<input type="text"/>	total nights spent in hospital

H.22 In the last 12 months have you been admitted to hospital (spent at least one night) for a reason other than your lung problems?

Yes No If no, please go to question H.24

H.23 If yes how many times? *(please use table provided to help you)*

admissions in last 6 months
 total nights spent in hospital

Admission	No. of nights
1 st	
2 nd	
3 rd	
Total	

H.24 During the last 12 months did you ever attend casualty or A & E for your lung problems?

Yes No If no, please go to question H.26

H.25 If yes, how many times?

times in the last 3 months Times in the last 12 months

H.26 During the last 12 months did you ever attend as a patient at the casualty or A & E department of a hospital for a reason other than your lung problems?

Yes No

H.27 If yes, how many times?

times in the last 3 months times in the last 12 months

Finally, please tick one of the below boxes

- I completed this questionnaire myself
- Someone else has completed this questionnaire on my behalf

Thank you for taking the time to complete this survey

The Birmingham COPD Cohort

Part of the Birmingham Lung Improvement StudieS (BLISS) programme



Baseline questionnaire

INTERVIEWER – LED SECTIONS

Patient Initials	
Study ID	
Date	
Interviewer ID	

Section 1: Background and Home Information

I.1 Please could I make a note of your medications:

Inhalers

DRUG NAME	DOSE	FREQUENCY	AILMENT

Other respiratory medications

DRUG NAME	DOSE	FREQUENCY	AILMENT

Other medications (Do not forget medications such as puffers, patches or eye drops)

DRUG NAME	DOSE	FREQUENCY	AILMENT

Section 2: Your work

I.2.1 Are you currently working in paid employment or self-employed?

Yes

No ***If NO, please go to question I.2.11***

I.2.2 If currently in employment, what is the full title of your main job, e.g. primary school teacher, registered nurse, car mechanic, television service engineer, benefits assistant. If you are a civil servant or local government officer, please give your job title, not your grade or pay band.

I.2.3 Describe what work you mainly do in your main job. Please describe as fully as possible.

I.2.4 Please give the name of your employer

I.2.5 Please briefly describe the nature of their work

Interviewer to record occupational code here

Does occupational code need double checking? Yes No

I.2.6 Is this a job you have done for most of your working life?

Yes ***Go to self-completion booklets***

No

I.2.7 If this is not the job you have done for most of your working life, what is the full title of your previous main job?

I.2.8 Describe what work you mainly did in your main job. Please describe as fully as possible.

I.2.9 Please give the name of your employer

I.2.10 Please briefly describe the nature of their work

Interviewer to record occupational code here

Does occupational code need double checking? Yes No

I.2.11 If you are not in work, have you ever been in paid employment?

Yes **Go to question. I.2.12**

No **Go to self-completion booklets**
I.2.12 When you were working what was the full title of your previous main job?

I.2.13 Describe what work you mainly did in your main job. Please describe as fully as possible.

I.2.14 Please give the name of your employer

I.2.15 Please briefly describe the nature of their work

Interviewer to record occupational code here

Does occupational code need double checking? Yes No

Thank you for taking the time to complete this survey

The Birmingham COPD Cohort
Part of the Birmingham Lung Improvement
StudieS (BLISS) programme



Baseline questionnaire

"NOT CURRENTLY IN WORK" BOOKLET

Your answers and opinions are valuable to us. We would be very grateful if you could read the below before turning the page:

- Please complete this questionnaire yourself if at all possible
- Please answer all questions as well as you can
- Do not spend too long thinking about your answers
- If someone is completing this on your behalf, they should record your answers

Patient Initials

Study ID

Date

N.1.1 Have you ever worked?

Yes

No ***If no, please go to N1.9***

NOT IN WORK (BUT HAVE WORKED)

N.1.2 Why did you stop work?

- Retired
- To look after the family or home
- Due to my lung problems
- Due to other health reasons
- Redundancy
- Other (please specify) _____

N.1.3 In which year did you stop working?

N.1.4 Which of the phrases below best described your last job? (*tick one box only*)

- Permanent
- Temporary – with no agreed end date
- Fixed period – with an agreed end date

N.1.5 What were your basic or contractual hours each week in your job at this workplace, excluding any paid or unpaid overtime?

Contracted Hours per week (to nearest hour)

N.1.6 How many hours did you usually work each week, including overtime or extra hours?

Usual hours per week (to nearest hour)

N.1.7 How much did you get paid for your job here, before tax and other deductions are taken out? If your pay before tax changed from week to week because of overtime, or because you work different hours each week, think about what you earn on average (*as with all information you give in this questionnaire, this will be treated with complete confidentiality*)

£50 or less per week	£2,600 or less per year	==
£51-£80 per week	£2601-£4160 per year	==
£81-£110 per week	£4161-£5720 per year	==
£111-£140 per week	£5721-£7260 per year	==
£141-£180 per week	£7,281-£9360 per year	==
£181-£220 per week	£9,361-£11,440 per year	==
£221-£260 per week	£11,441-£13,520 per year	==
£261-£310 per week	£13,521-£16,120 per year	==
£311-£360 per week	£16,121-£18,720 per year	==
£361-£430 per week	£18,721-£22,360 per year	==
£431-£540 per week	£22,361-£28,080	==
£541-£680 per week	£28,081- £35,360 per year	==
£681-£870 per week	£35,361-£45,240 per year	==
£871 or more per week	£45,241 or more per year	==
Prefer not to say		==

N.1.8 Are you currently:

- At a college or training centre
- Looking after the family or home
- Voluntary worker
- Actively seeking work
- On any kind of government training scheme
e.g. work-based learning for adults, or New Deal for 50+?
- None of the above

Now please go to N1.11

NEVER WORKED: If you have never worked,

N.1.9 is this because of:

- Your health
- Other reason(e.g. looking after family)

N.1.10 Are you:

- At a college or training centre
- Looking after the family or home
- Voluntary worker
- Actively seeking work
- On any kind of government training scheme
e.g. work-based learning for adults, or New Deal for 50+?
- None of the above

N.1.11 Nowadays, what is your usual gross household income? Please include the value of any welfare benefits, pensions, investments, rents, contributions from relatives) (*as with all information you give in this questionnaire, this will be treated with complete confidentiality*)

Tick one box only

£50 or less per week	£2,600 or less per year	<input type="checkbox"/>
£51-£80 per week	£2601-£4160 per year	<input type="checkbox"/>
£81-£110 per week	£4161-£5720 per year	<input type="checkbox"/>
£111-£140 per week	£5721-£7260 per year	<input type="checkbox"/>
£141-£180 per week	£7,281-£9360 per year	<input type="checkbox"/>
£181-£220 per week	£9,361-£11,440 per year	<input type="checkbox"/>
£221-£260 per week	£11,441-£13,520 per year	<input type="checkbox"/>
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£361-£430 per week	£18,721-£22,360 per year	<input type="checkbox"/>
£431-£540 per week	£22,361-£28,080	<input type="checkbox"/>
£541-£680 per week	£28,081- £35,360 per year	<input type="checkbox"/>
£681-£870 per week	£35,361-£45,240 per year	<input type="checkbox"/>
£871 or more per week	£45,241 or more per year	<input type="checkbox"/>
Prefer not to say		<input type="checkbox"/>

Finally, please tick one of the below boxes

- I completed this questionnaire myself
- Someone else has completed this questionnaire on my behalf

Thank you for taking the time to complete this survey

Appendix 4 Development of the Birmingham Lung Improvement Studies prognostic score for chronic obstructive pulmonary disease patients in primary care: data from the Birmingham chronic obstructive pulmonary disease cohort

Development of the Birmingham Lung Improvement Studies (BLISS) prognostic score for COPD patients in primary care: data from the Birmingham COPD cohort

ABSTRACT

Introduction

COPD patients in primary care have high rates of hospital admissions. A prognostic score could be used to guide patient management and reduce risk of admission but currently available scores do not perform well enough and are not used in practice.

Methods

Using data from the Birmingham primary care COPD cohort we developed and internally validated a new prognostic score from 25 candidate variables considered important from the literature and a patient-clinician stakeholder group. 1558 patients on COPD registers of 71 GP practices and 331 newly-identified patients identified from a linked case-finding trial were included and their self-reported and clinical data linked to routine hospital episode statistics. The primary outcome was the record of at least one respiratory admission within 2 years of cohort entry (May 2012-June 2014) and the secondary outcome included full follow-up data up to 01/04/2016. The model was developed using backward elimination with $p < 0.157$. Fractional polynomials were considered and multiple imputation using chained equations was used for missing data. Discrimination was assessed using the c-statistic and calibration was also assessed. Bootstrapping was used for internal validation and the optimum-adjusted performance statistics were presented.

Results

Median (min, max) follow up was 2.9 years (1.8, 3.8). Of 25 candidate variables, 9 were retained in the final developed model including age, sex, smoking status, CAT score, respiratory admissions in the previous 12m, BMI, diabetes, FEV1Q and FEV1/h₂. After adjustment for optimism, the primary model performed well in predicting 2yr respiratory admissions (c statistic=0.80 (95%CI 0.77, 0.83) and calibration slope 0.88 (0.75, 1.01)). Three further variables were included in the secondary analysis but with similar score performance.

Conclusions

The BLISS score has better performance in predicting respiratory admissions than the scores currently available. All 9 variables are readily available in primary care records or would be easy to collect, and a simple computer programme could calculate the score. Important next steps are external validation, proposing and evaluating a model of use to guide patient management and exploration of the best ways to implement such a score in primary care practice.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most common long-term conditions managed in primary care [1,2], and is also one of the most expensive to healthcare systems with a high rate of hospital admissions due to exacerbations of the condition [3,4]. In many countries there are policies and incentives to keep patients out of hospital where possible [5,6], which would benefit both the patients and the health system; however the rates of hospital admissions for this condition have not declined [7] and better strategies are urgently needed.

Prognostic scores (or indices) are often used in medical practice to assess and communicate patient risk and guide the management of individual patients, or stratify care at a practice level [8]. In the case of COPD, there are a large number of proposed prognostic scores [9,10], including the more well-known ones such as the BODE index [11], the DOSE index [12] and the ADO score [13]. These multicomponent scores have been shown to predict prognosis better than single components such as airflow obstruction, especially for predicting mortality where the ADO score has been recently shown to be the best performing score, followed by the BODE index [9]. However, none of these scores are routinely used in practice because of limitations in the development methodology, lack of validation in appropriate populations, impracticality of obtaining the variables or lack of consideration for the most important clinical outcomes. This is particularly relevant for primary care settings, where some of the proposed clinical measures may not be routinely available or practical to measure [9,10].

However, despite the large number of proposed indices, a recent systematic review revealed the lack of suitable prognostic score for predicting hospital admissions, one of the most pertinent outcomes for primary care [10]. The need for a good quality and useful prognostic score is highlighted in the latest UK NICE guidance consultation [14]. In this paper, we present the development of a new prognostic score, the BLISS score, derived from a specifically recruited primary care COPD cohort in the West Midlands region of the UK [15]. This cohort also includes case-found patients from a linked trial [16], and therefore uniquely represents both traditionally diagnosed and newly identified patients.

METHODS

This paper was written in accordance with the TRIPOD statement [17].

Aims and objectives

Development and internal validation of a new prognostic score to predict acute respiratory hospital admissions among COPD patients, for use in primary care, using data from the Birmingham COPD cohort.

Population and setting

The details of the Birmingham COPD cohort have been described in a previous publication.[15]

The cohort comprises three groups of participants: (1) 1558 COPD patients aged 40 years and over identified from the Quality and Outcomes Framework (QOF) COPD registers of 71 UK general practices within the West Midlands region of the UK; (2) 331 newly detected COPD patients aged 40-79 years from 54 of the 71 practices, identified through a linked case-finding trial (i.e. incident cases) [16]; (3) 413 patients with relevant chronic respiratory symptoms but without airflow obstruction (ie symptomatic normals), also recruited through the TargetCOPD trial [16]. This analysis includes prevalent and incident COPD cases only. Baseline assessments took place at cohort entry (31 May 2012 to 25 June 2014) and follow-up assessments took place from 2015-2016, with linked hospital episode data obtained through the Health and Social Care Information Centre (HSCIC) for the period 1 April 2012 to 31 March 2016.

Potential participants to the cohort were invited to take part by their GP, or directly from the investigators if they had provided consent through the trial, with up to two reminders for non-responders. Informed consent was obtained at the initial face-to-face visit.

Candidate variables

A large pool of potential candidate variables were identified from the literature, including variables used in relevant published prognostic scores and variables shown to be individually prognostic. A final set of candidate variables was selected through discussion with a consensus panel of study investigators/clinicians to take into consideration likely contribution to the model, accuracy and practicality in collecting the data in the primary care setting (table 1). The variables were collected from within the cohort study assessments and questionnaires and linked hospital episode statistics.

Data collection within the cohort study

At cohort entry, participants completed a face-to-face baseline clinical assessment and several self-reported questionnaires including socio-demographic variables (age, sex, ethnicity, smoking status, social contact), disease specific variables (number of exacerbations in the previous 12 months (estimated by courses of steroids and antibiotics taken), presence of chronic bronchitis [18], extent of dyspnoea (MRC scale) [18]) and selected physician-diagnosed conditions. Disease-specific health-related quality of life (HRQL) was measured using the COPD assessment test (CAT)[19] and general health using a 5-point Likert scale. Self-reported exercise levels were reported using the IPAQ-short [20] and exercise capacity measured using the sit-to-stand test[21]. Height was measured to the nearest 0.1 cm using a Leicester height monitor, and weight (to the nearest 0.1 kg) was assessed using the Tanita BC-420SMA body composition scale.

Lung function (FEV₁) was measured using the nddEasy One Spirometer (nnd, Switzerland), administered by researchers trained to ARTP Foundation Spirometry Certificate standard [15] before (max eight blows) and after (max six blows) 400µg salbutamol, stopping when repeatability within 100mls was achieved. The highest recording was then taken. FEV₁% predicted was estimated using the GLI equations [22]. Due to the documented statistical problems with the use of the FEV₁% predicted measure, we examined 3 different measures of FEV₁ as potential predictors: FEV₁Q, FEV₁/height² and FEV₁% predicted [23]. Bronchial hyper-responsiveness was defined as change between pre & post BD FEV₁ >12% and >200ml, OR change between pre & post BD FVC₁ >12% and >200ml. The IMD (2010) score was calculated as a measure of deprivation, based on patients' individual postcode [24].

We obtained data on current or main occupation using a questionnaire administered by trained research assistants, who used information on skill content and skill level to assign a 4-digit standard occupational classification (SOC 2010) [25] code using the CASCOT (computer assisted structured coding tool) software.[26] Risk of occupational exposure to vapours, gases, dust and fumes (VGDF) was derived using a job exposure matrix [27], modified for use with SOC 2010 codes.

Use of cardiovascular medications was self-reported by patients.

Outcomes

Data on hospital episodes were obtained from NHS Digital using patient NHS number and linked to the cohort data via a unique study ID. The primary outcome was one or more acute

respiratory admissions during the two year period since entry to the cohort, defined using specific respiratory ICD10 codes (see Appendix 1). As a sensitivity analysis, we developed a prognostic model to predict occurrence of one or more acute respiratory admissions during the full follow-up period from cohort entry until the NHS Digital admissions data was obtained (01/04/2016).

Statistical analyses

Developing the prognostic model

The outcome was modelled using a logistic regression model. Firstly the full model was fitted, including all candidate variables, and then backward elimination performed, with a conservative significance level of 0.157 used [28]. For categorical variables included in the model, the category with the lowest p-value was used to assess the significance level. No variables were forced into the model. Continuous variables remained in their raw form to ensure data were not lost through dichotomisation. Initially a linear trend was assumed, then, where possible, fractional polynomials were considered (set of powers considered: -2, -1, -0.5, natural logarithm, 0.5, 1, 2, 3) with $p < 0.001$ indicating the use of a fractional polynomial rather than linear trend. [29] Fractional polynomials were also used for the continuous variables eliminated from the model to check whether they should be included in the fractional polynomial format.

Multiple imputation (using chained equations) was used for all variables considered in the model and auxiliary variables used to aid the imputation. The number of imputed data sets used was equal to the fraction of missing data (64 data sets for 64% missing data). [30]

Assessment of prognostic model performance

Assessment of the fitted model was achieved by estimating calibration and discrimination. A calibration plot was produced by plotting the observed risk against the predicted risk and the calibration slope calculated. To judge discrimination the area under the receiver operating curve was calculated (equivalent to the c-statistic).

Internal validation of the prognostic model

This developed ‘apparent’ model was then internally validated using bootstrap methods. Each imputed dataset was used to generate 100 bootstrapped datasets. Each one of these bootstrapped data sets was then used to develop a prognostic model in the same way as the original model. Estimates of performance (c-statistic and calibration slope) were obtained

from the model fitted using each of the bootstrapped data sets. The estimates obtained from the bootstrapped data sets were averaged and subtracted from the estimates from the original model to estimate optimism and provide optimism-adjusted performance statistics.

Final prognostic model

The optimised adjusted calibration slope was then used as a uniform shrinkage factor. Each of the coefficients from the original apparent model was adjusted by multiplying by the shrinkage factor. The intercept was also adjusted to ensure calibration-in-the-large.

Subsidiary and sensitivity analyses

Although the final model included two different measures of FEV₁, we also considered how the inclusion of only one of the three potential measures would impact on the model performance by evaluating their separate inclusion at the development stage within the apparent model. We also evaluated how well the model would perform on the prevalent cases only.

Sample size calculation

With 267 events for the primary outcome, up to 26 candidate variables could be used, based on the rule of thumb of 10 events per candidate variable. [31]

RESULTS

Characteristics of participants

Of 7176 invited to the cohort, 1558 prevalent and 331 incident participants completed baseline assessments and were included in these analyses [15]. Median follow-up (min, max) was 2.9 years (1.8, 3.8 years), 382 (16%) had a respiratory admission recorded during the study period, and 267 (12%) had a respiratory admission in the primary two year period. Participants with hospitalisations were more likely to be older (70.6 vs 6.7 years, $p<0.001$), male (65% vs 59% $p=0.017$), more deprived (median IMD score 30.7 vs 23.8, $p<0.001$), have lower BMI (mean 28.1 vs 28.9, $p=0.017$), more severe airflow obstruction (mean FEV1 55.2 vs 76.8% predicted), worse dyspnoea (MRC 3-5 74% vs 49%, $p<0.001$), worse quality of life scores (median CAT score 24 vs 16, $p<0.001$), report previous exacerbations (62% vs 42%, $p<0.001$) and previous hospitalisations (16.0% vs 2.2%, $p<0.001$), higher rate of VGDF (71% vs 62%, $p=0.001$) and smoking exposure (31.8% vs 26.5% current smokers, $p<0.001$), and have diabetes (24% vs 15%, $p<0.001$) and cardiovascular disease (22% vs 14% with coronary heart disease, $p<0.001$) (Table 2).

Primary analysis predicting acute respiratory admissions in a 2-year period

For the primary analysis, of 25 candidate predictors, 9 were retained in the final developed model (table 3), including age, sex, smoking status, CAT score, previous respiratory admission, BMI, self-report of a diagnosis of diabetes and two different measures of obstruction. After adjusting for optimism (using a uniform shrinkage factor of 0.869), the prediction model was able to discriminate between COPD participants with and without a respiratory admission with a c-statistic of 0.80 (0.77, 0.83) (table 4). There was also good agreement between observed and predicted probabilities with a calibration slope of 0.88 (0.75, 1.01) (fig 1).

Sensitivity analysis predicting acute respiratory admissions for the full follow-up

We repeated the analysis using the full follow-up period. An additional 3 variables were retained in the model (antibiotic/steroid prescription in the last 12 months, bronchial hyper-responsiveness and self-report of a diagnosis of heart failure) were retained in the final developed model (Table S1). After adjusting for optimism (shrinkage factor 0.877) the c-statistic was similar at 0.80 (0.78, 0.83), again with good agreement between observed and expected probabilities (fig S1).

Further sensitivity analyses

At the initial model development stage (the apparent model), we explored the use of only one measure of airflow obstruction. With only FEV_Q included the c-statistic was 0.77 (0.74, 0.80); with only FEV_{1/h2} the c-statistic was 0.78 (0.75, 0.81) and with only FEV_{1%} predicted, the c-statistic was 0.78 (0.75, 0.81). Including only prevalent cases resulted in a c-statistic of 0.76 (95%CI: 0.73 to 0.79). These results were not adjusted for optimism.

Examples of the application of this score (see Table 3 for equation)

Example 1 – A 70 year old male, who is a current smoker, has a BMI of 20, and has had a respiratory related hospitalisation in the previous 12 months. His obstruction is measured as 0.25 (FEV_{1/h2}) and 8 (FEV_{1q}). His disease specific HRQL category is 35, and he does not have diabetes. He has a predicted risk of 83.4% of having a respiratory related hospitalisation in the next two years. *Interpretation:* If 1000 people with the same risk factors are followed for two years, 834 would have a respiratory related hospitalisation.

Example 2 – A 60 year old female, who has never smoked, has a BMI of 25, and has not had a previous respiratory related hospitalisation in the previous 12 months. Her obstruction is measured as 0.1 (FEV_{1/h2}) and 4 (FEV_{1q}). Her disease specific HRQL category is 20, and she has diabetes. She has a predicted risk of 13.5% of having a respiratory related hospitalisation within two years. *Interpretation:* If 1000 people with the same risk factors are followed for two years, 135 would have a respiratory related hospitalisation.

DISCUSSION

Key findings

Although there are more than 27 proposed prognostic models and scores in the published literature evaluated for use in predicting exacerbations of COPD, none of these are suitable for use in practice because of limitations in the methodology of their development or validation, inadequate performance in predicting hospital admissions (indicating that further variables are needed) or impracticality in measuring some components in primary care. [10] We have used data from a unique primary care COPD cohort to develop a novel prognostic score for primary care, considering all the potential predictors from previously published scores and other prognostic factors likely to be important. Using best practice methodology we have produced the BLISS score, which has good discriminative ability and good calibration and better performance than any previously published scores in predicting risk of respiratory admissions [10]. There are 9 variables, all readily available in primary care records or easy to collect and each of the components has been shown to be individually associated with increased risk of admission and therefore not a surprising inclusion. Age and respiratory admission in the previous 12 months were strong predictors in the model, which is consistent with other evidence [32,33]. BMI is known to have a non-linear relationship with poor prognosis [34], which may also explain its non-linear function in our score.

Comparison with existing literature

The BLISS score has many variables in common with other prognostic scores for COPD. Airflow obstruction is the most commonly found variable, followed by previous exacerbations, age, smoking, COPD-specific quality of life, BMI and sex [10]. The most commonly known scores have been developed to predict other outcomes such as mortality or health-related quality of life [9]. Of these, the BODE index contains two of the BLISS score variables (BMI, obstruction) but dyspnoea and exercise capacity rather than the CAT score. [11] The DOSE index contains three of the BLISS index variables (obstruction, smoking status and exacerbations) [12] and the ADO score contains age and obstruction in common [13], but both also contain dyspnoea as well. It is likely that the CAT score and the MRC score measure similar dimensions (impact of breathlessness) and they are frequently used as alternatives to each other [35]. A number of scores also include comorbidities [36-38] although none identify diabetes as a single predictive component. Very few scores have been developed within a primary care setting. However, the most relevant comparative score is

probably that produced by Bertens et al [36] which aimed to predict exacerbations (described by steroid use or hospitalisation) in a 2-year period among COPD patients in primary care. This score, containing 4 variables (previous exacerbations, FEV1% predicted, pack years of smoking and presence of vascular disease), was derived within a primary care cohort of COPD patients aged 65 years and over from 51 general practices in the Netherlands, and validated in a cohort aged 50 years and over. Although having good discrimination and good calibration in the derivation cohort ($c=0.75$) it had moderate discrimination in the validation cohort (c -statistic of 0.66 (95% CI: 0.62–0.71), considered a more limited range of candidate variables and defined exacerbations more broadly as those requiring courses of antibiotics or steroids or hospital admissions.

Limitations of this study

Although the BLISS score is based on 9 readily available or easily obtainable components, the non-linear nature of several of them makes it more difficult to understand and compute than a simple points-based score. However, most GP systems have an inbuilt facility to calculate such scores, or a simple programme in Excel could do this.

Many of the components are based on self-report, which for comorbidities may not be as accurate as data available in routine GP records, although is unlikely to be systematically biased.

In the UK, the CAT score is less commonly recorded than the MRC score (which is required for QOF), although it is suggested to be collected during annual reviews [39] and appears to be more useful for prognosis and would not be difficult to collect and record as it consists of only eight questions on a Likert scale.

There has been considerable debate about the value of including non-modifiable factors such as age in COPD prognostic scores. However, excluding important predictive factors such as age and sex would lead to confounding and biased estimates of the remaining predictors, producing a score which performs badly. The aim of a prognostic score should be to predict risk accurately; the role of the clinician is to then use the score to guide their management, which can address the factors which are modifiable.

The inclusion of two different measures of FEV1 may be considered unusual. Due to controversies surrounding the best potential measure [23], we considered three different possibilities and allowed the statistical approach to determine which was more useful. The best combination included both FEV1/height² and FEV1Q. These capture slightly different

dimensions where the FEV1/height² standardises for a person's size, and the FEV1Q is an index of the number of turnovers of a nominal lower limit of lung function remaining, and takes into account some sex and size differences in lung function [23]. This is consistent with another study suggesting that FEV1Q and FEV1/h₂ were the best measures to use [40]. However, our sensitivity analyses showed that including only one at a time reduced the overall performance of the score a little, although of the 3 single measures, the traditional FEV1% predicted performed the best.

Most of the included participants had 2 years of follow-up data which provided the primary outcome. Our secondary analyses included full follow-up data (median 2.9 years), an extra 115 events and a further 3 variables although these contributed less to the model than the original variables and were probably included due to the increased statistical power available. Most previous studies have follow-up limited to one year [10].

Finally, it is possible that our population does not truly represent primary care as we included those who were case-found, and also those who were prepared to take part in a research study who would be more likely to have milder disease than the average of primary care [15]. Indeed the score performed slightly less well amongst prevalent-only cases, although this was not statistically significant.

Implications for research and practice

Although we have performed internal validation, before the score should be used, further external validation in relevant primary care datasets is important. Further work with primary care clinicians is also needed to understand the reasons for lack of uptake of such scores in practice, and then using this information to propose and test a practical use for the score in guiding or stratifying patient management. [41]

It is possible that a whole practice COPD population could be stratified by 2-year risk of admission, and then the greatest resources directed towards those at greatest risk. Trials which test this approach are needed. A further use might be to guide individual patient management. Within the GOLD guidelines, the new ABCD matrix includes one dimension which relates to exacerbation risk [35]. At the moment, that exacerbation risk is defined by number of previous exacerbations. Perhaps the BLISS score could be used as a better marker of future risk? However it would be important to decide how to categorise level of risk within the BLISS score, and how many cut-points it should have.

There are now many such scores available, and given our rigorous approach and the fact that the score has both good discrimination and calibration, now it is time to move to the next phase and test its utility in practice rather than developing new scores.

Conclusions

Using robust methodology and a COPD patient cohort which represents primary care, we have developed and internally validated a new prognostic score which performs very well in predicting respiratory admissions within a two-year timeframe. The components are easy to collect and the score performs better than any other published score. The next steps are to test its application in practice and identify how best to implement its use in a real life primary care setting.

REFERENCES

1. Halbert RJ, Natoli JL, Gano A, et al. Global burden of COPD: systematic review and meta-analysis. *The European Respiratory Journal* 2006;28(3):523-32.
2. Quality and Outcomes Framework 2013/14. Available from: <http://www.hscic.gov.uk/catalogue/PUB15751>
3. Mahon J, Bartlett C, Isojarvi J, Edwards M, Glanville J. York Health Consortium YH. Literature review: the economic costs of lung disease and the cost-effectiveness of policy and service interventions. 2017 Oct 2017. <https://www.brit-thoracic.org.uk/document-library/research-and-innovation/documents/literature-review-the-economiccosts-of-lung-disease/>
4. McLean S, Hoogendoorn M, Hoogenveen RT, Feenstra TL, Wild S, Simpson CR, et al. Projecting the COPD population and costs in England and Scotland: 2011 to 2030. *Sci Rep*. 2016;6:31893
5. Department of Health (England). Improving the health and well-being of people with long-term conditions. Department of Health; 2010.
6. Department of Health (England). An outcomes strategy for people with chronic obstructive pulmonary disease (COPD) and asthma in England. 2011
7. Hospital Episode Statistics, Admitted Patient Care, England - 2013-14. Available from: <http://www.hscic.gov.uk>
8. Moons KGM, Altman DG, Vergouwe Y, Royston P. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. *BMJ* [Internet] 2009;338(7709):1487–1490. Available from: <http://www.bmj.com/cgi/doi/10.1136/bmj.b606>
9. Guerra B, Haile SR, Lamprecht B, et al. Large-scale external validation and comparison of prognostic models: An application to chronic obstructive pulmonary disease. *BMC Med* 2018;16(1):1–13
10. Guerra B, Gaveikaite V, Bianchi C, et al. Prediction models for exacerbations in patients with COPD. *Eur Respir Rev* 2017; 26: 160061 [https://doi.org/10.1183/16000617.0061-2016].
11. Celli B, Cote C, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* [Internet] 2004;350(10):1005–12. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14999112>

12. Jones RC, Donaldson GC, Chavannes NH, et al. Derivation and validation of a composite index of severity in chronic obstructive pulmonary disease: The DOSE index. *Am J Respir Crit Care Med* 2009;180(12):1189–1195.
13. Puhan MA, Hansel NN, Sobradillo P, et al. Large-scale international validation of the ADO index in subjects with COPD: an individual subject data analysis of 10 cohorts. *BMJ Open* 2012;2:e002152. doi:10.1136/bmjopen-2012-002152
14. <https://www.nice.org.uk/guidance/indevelopment/gid-ng10026/documents>
15. Adab P, Fitzmaurice DA, Dickens AP, et al. Cohort Profile: The Birmingham Chronic Obstructive Pulmonary Disease (COPD) Cohort Study. *Int J Epidemiol* [Internet] 2016;46(1):dyv350. Available from: <https://academic.oup.com/ije/article-lookup/doi/10.1093/ije/dyv350>
16. Jordan RE, Adab P, Sitch A, et al. Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial. *Lancet Respir Med* [Internet] 2017;4(9):720–730. Available from: [http://dx.doi.org/10.1016/S2213-2600\(16\)30149-7](http://dx.doi.org/10.1016/S2213-2600(16)30149-7)
17. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): The TRIPOD Statement. *Ann Intern Med* 2017;162(1):55–63.
18. Fletcher CM. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). *British Medical Journal* 1960;(2):1665.
19. Jones PW, Harding G, Berry P, et al. Development and first validation of the COPD Assessment Test. *The European Respiratory Journal* 2009;34(3):648–54.
20. Craig CL, Marshall AL, Sjoström M et al. International physical activity questionnaire: 12-country reliability and validity. *Medicine and science in sports and exercise* 2003;35:1381–95.
21. Ozalevli S, Ozden A, Itil O, Akkoçlu A. Comparison of the Sitto-Stand Test with 6 min walk test in patients with chronic obstructive pulmonary disease. *Respir Med* 2007;101:286–93.
22. Quanjer PH, Stanojevic S, Cole TJ, et al. ERS Global Lung Function Initiative. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *Eur Respir J* 2012; 40: 1324–43.

23. Miller et al. New concepts for expressing forced expiratory volume in 1 s arising from survival analysis *Eur Respir J* 2010; 35: 873–882. DOI: 10.1183/09031936.00025809FEV1/h2
24. Department for Communities and Local Government. English Indices of Deprivation 2010. <http://data.gov.uk/dataset/index-of-multiple-deprivation-2010> [cited 2015 Apr 14]
25. SOC 2010. <https://www.ons.gov.uk/methodology/classificationsandstandards/standardoccupationalclassification/soc/soc2010>
26. Warwick Institute for Employment Research. CASCOT: Computer Assisted Structured Coding Tool. <http://www2.warwick.ac.uk/fac/soc/ier/software/cascot/> 2014
27. Sadhra SS, Kurmi OP, Chambers H, et al. Development of an occupational airborne chemical exposure matrix. *Occupational Medicine* 2016;66(5):358-64.
28. Sauerbrei W. The use of resampling methods to simplify regression models in medical statistics. *Journal of the Royal Statistical Society Series C-Applied Statistics*. 1999;48:313-29.
29. Thangaratinam S, Allotey J, Marlin N, Mol BW, Von Dadelszen P, Ganzevoort W, Akkermans J, Ahmed A, Daniels J, Deeks J, Ismail K. Development and validation of Prediction models for Risks of complications in Early-onset Pre-eclampsia (PREP): a prospective cohort study. *Health Technol Assess*. 2017.
30. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine*. 2011;30(4):377-99 Peduzzi
31. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996 Dec 1;49(12):1373-9.
32. Motegi T, Jones RC, Ishii T, et al. A comparison of three multidimensional indices of COPD severity as predictors of future exacerbations. *Int J COPD* 2013; 8: 259–271.
33. Hurst JR, Vestbo J, Anzueto A, et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med* 2010; 363: 1128–1138.
34. Guo Y, Zhang T, Wang Z, et al. Body mass index and mortality in chronic obstructive pulmonary disease: A dose–response meta-analysis. Liu. J, ed. *Medicine*. 2016;95(28):e4225. doi:10.1097/MD.0000000000004225.
35. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease. GOLD, 2018.

https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf

36. Bertens LC, Reitsma JB, Moons KG et al. Development and validation of a model to predict the risk of exacerbations in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2013;8:493–99.
37. Almagro P, Barreiro B, Ochoa de Echaguen A, et al. Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration* 2006; 73: 311–317.
38. Amalakuhan B, Kiljanek L, Parvathaneni A, et al. A prediction model for COPD readmissions: catching up, catching our breath, and improving a national problem. *J Community Hosp Intern Med Perspect* 2012; 2: 9915.
39. NICE quality standards. <https://www.nice.org.uk/guidance/qs10>
40. Tang-Hsiu Huang, Tzuen-Ren Hsiue, Sheng-Hsiang Lin, Xin-Ming Liao, Po-Lan Su, Chiung-Zuei Chen *European Respiratory Journal* 2018 51: 1700577; DOI: 10.1183/13993003.00577-2017
41. van Dijk WD, van den Bemt L, van den Haak-Rongen S, Bischoff E, van Weel C, in ‘t Veen JCCM, Schermer TRJ. Multidimensional prognostic indices for use in COPD patient care. A systematic review. *Respiratory Research* 2011, 12:151
<http://respiratory-research.com/content/12/1/151>

Table 1 Candidate variables and data source

Description	Form of variable	Data source
Demographics		
BMI	Categorical	Cohort assessment data
Age	Continuous	Cohort self-report data: questionnaires
Sex	Binary	Cohort self-report data: questionnaires
Ethnicity	Categorical	Cohort self-report data: questionnaires
COPD specific risk factors		
Obstruction—FEV1 % predicted	Continuous	Cohort assessment data
Obstruction—FEV1Q*	Continuous	Cohort assessment data
Obstruction—FEV1/height ²	Continuous	Cohort assessment data
Bronchial hyper-responsiveness	Binary	Cohort assessment data
Dyspnoea—MRC scale	Categorical	Cohort self-report data: questionnaires
Disease specific HRQL – CAT	Continuous	Cohort self-report data: questionnaires
Previous respiratory hospitalisations (12 months prior to baseline)	Binary	NHS Digital
Course of antibiotics/steroids within last 12 months	Binary	Cohort self-report data: questionnaires
Chronic cough and/or chronic phlegm for 3 or more months of the year	Binary	Cohort self-report data: questionnaires
Other risk factors		
Smoking	Categorical	Cohort self-report data: questionnaires
Social isolation	Binary	Cohort self-report data: questionnaires
Exercise capacity—sit to stand test	Continuous	Cohort assessment data
Physical activity—IPAQ	Categorical	Cohort self-report data: questionnaires
History of CVD	Binary	Cohort self-report data: questionnaires
Medication for CVD	Binary	Cohort self-report data: questionnaires
Heart failure	Binary	Cohort self-report: questionnaires
Asthma	Binary	Cohort self-report data: questionnaires
Depression	Binary	Cohort self-report data: questionnaires
Diabetes	Binary	Cohort self-report data: questionnaires
Any cancer	Binary	Cohort self-report data: questionnaires
Osteoporosis	Binary	Cohort self-report data: questionnaires

*See Miller et al [23] for calculation

Table 2: Baseline characteristics of BLISS cohort study participants by respiratory hospitalisation during study period.

Variable	Total population (N =2,305)	No hospitalisation (N = 1,923)	Respiratory hospitalisation (N = 382)	P-value ¹
Demographics				
Age, Mean (SD)	67.4 (9.9)	66.7 (9.7)	70.6 (10.2)	<0.001
Sex (Male)	1,382 (60)	1,132 (59)	250 (65)	0.017
Ethnicity				
White British	1,918 (83.2)	1,601(83.3)	317(83.0)	0.525
Asian	53 (2.3)	47(2.4)	6(1.6)	
African/Caribbean	23 (1.0)	20(1.0)	3(0.8)	
Mixed	13 (0.6)	10(0.5)	3(0.8)	
Other	120 (5.2)	94(4.9)	26(6.8)	
Unclear/Missing	178 (7.7)	151(7.9)	27(7.1)	
Deprivation (IMD), median [IQR]	25.0 [14.4 to 41.4]	23.8 [14.1 to 39.7]	30.7 [17.1 to 45.1]	<0.001
BMI, mean (SD)	28.7 (5.8)	28.9 (5.5)	28.1 (6.7)	0.017
COPD specific				
Obstruction (FEV1% predicted) , median [IQR]	73.7 [56.7 to 88.8]	76.8 [60.9 to 90.9]	55.2 [38.9 to 72.2]	<0.001
Obstruction (FEV1 Q) , median [IQR]	0 [0 to 2]	0 [0 to 2]	2 [0 to 4]	<0.001
Obstruction (FEV1/h2) , mean (SD)	0.69 (0.27)	0.73 (0.26)	0.52 (0.23)	<0.001
Bronchial hyper-responsiveness	155 (6.7)	121 (6.3)	34 (8.9)	0.063
Dyspnoea				
Grade 1 – 2	1,014 (47)	920 (51)	94 (26)	<0.001
Grade 3 – 5	1,157 (53)	895 (49)	262 (74)	
Disease specific HRQL Categories, median [IQR]	17 [11 to 24]	16 [10 to 23]	24 [18 to 31]	<0.001
Respiratory hospitalisation in the previous 12m² (Count)				
0	2,202 (95.5)	1,881 (97.8)	321 (84)	<0.001
1	78 (3.4)	37 (1.9)	41 (10.7)	
2+	25 (1.1)	5 (0.3)	20 (5.2)	
Previous hospitalisation ² (Binary)	103 (4.5)	42 (2.2)	61 (16.0)	<0.001
Antibiotics/Steroids	1,040 (45)	802 (42)	238 (62)	<0.001
Chronic cough and/or chronic phlegm	1,332 (58)	1,072 (56)	260 (68)	<0.001
VGDF exposure	2,239 (63)	1,152 (62)	263 (71)	0.001
Other risk factors				

Smoking				
Never Smoker	268 (12.6)	246 (13.8)	22 (6.3)	<0.001
Current Smoker	583 (27.4)	472 (26.5)	111 (31.8)	
Ex Smoker	1,279 (60.0)	1,063 (59.7)	216 (61.9)	
Social isolation	130 (6)	100 (6)	30 (8)	0.048
Exercise capacity (Sit to stand test)	19 [15 to 23]	20 [15 to 24]	16 [13 to 20]	<0.001
Physical activity (IPAQ)				
Low Activity	730 (41)	580 (39)	150 (55)	<0.001
Moderate Activity	595 (34)	515 (34)	80 (30)	
High Activity	439 (25)	398 (27)	41 (15)	
General health (Likert scale)				
1	171 (7.8)	159 (8.7)	12 (3.4)	<0.001
2	848 (38.7)	769 (42.0)	79 (22.1)	
3	926 (42.3)	745 (40.6)	181 (50.7)	
4	215 (9.8)	143 (7.8)	72 (20.2)	
5	30 (1.4)	17 (0.9)	13 (3.6)	
Asthma	811 (40)	669 (39)	142 (44)	0.071
Depression	479 (24)	409 (24)	70 (22)	0.445
Diabetes	330 (16)	252 (15)	78 (24)	<0.001
Cancer	266 (13)	223 (13)	43 (13)	0.884
Osteoporosis	156 (8)	124 (8)	32 (11)	0.075
Cardiovascular disease related				
Coronary heart disease	30 (15)	235 (14)	73 (22)	<0.001
Heart failure	158 (8)	116 (7)	42 (13)	<0.001
Medication	1,152 (50)	924 (48)	228 (60)	<0.001

Values are Number (percentage) unless specified.

1: P-value obtained from t-test, Mann-whitney U test, or chi-squared test. 2: Hospitalisation for respiratory related problem in previous 12 months obtained from Hospital episode statistics . IQR: Inter-quartile range.

Table 3: Final multivariable model for risk of respiratory hospitalisation within two years for participants with chronic obstructive pulmonary disease

Variable	OR (95%CI)	β coefficients
FEV1/h ₂	0.131 (0.069 - 0.252)	-2.02928538
Disease specific HRQL Categories	1.045 (1.028 - 1.062)	0.04386269
Sex (Male)	1.402 (1.076 - 1.827)	0.33805492
Previous 12 month respiratory hospitalisation	3.882 (2.591 - 5.816)	1.35624740
Diabetes	1.550 (1.103 - 2.179)	0.43830211
None Smoker	Reference	-
Current Smoker	1.691 (0.979 - 2.921)	0.52533606
Ex Smoker	1.687 (1.022 - 2.782)	0.52265980
Fractional polynomial transformation		
(BMI/10) ₃		-0.13840965
BMI/10) ₃ x ln(BMI/10)		0.08650160
Age/10		-5.74991978
(Age/10) x ln(Age/10)		2.02527365
(FEV1Q + 0.000005)/100		0.53161365
((FEV1Q + 0.000005)/100) x ln((FEV1Q + 0.000005)/100)		-1.09589609
Constant		10.95740000

Risk score = 10.957 – 2.029FEV1h₂ + 0.044CAT + 0.338Male + 1.356previous hospitalisation + 0.438Diabetes + 0.525Current smoker + 0.523Ex smoker – 0.138((bmi/10)³)+0.087(bmi/10)³ln(bmi/10) – 5.750 Age/10 + 2.025 Age/10 ln(Age/10)+0.532 ((FEV1Q+ 0.000005)/100) – 1.096((FEV1Q+ 0.000005)/100)ln((FEV1Q+ 0.000005)/100).

Note: ln= natural logarithm

All variables are coded as binary (0 for absence of presence of a risk factor), except for FEV1/h₂, FEV1Q, HRQL, BMI, and Age. The value 10.957 is the intercept, and the other numbers reflect the estimated coefficients for the predictors, indicating their contribution to the risk. The regression coefficients represent the log odds ratio for a change in 1 unit in the corresponding predictor. The predicted risk of hospitalisation is 1/(1+e^{-riskscore}).

Table 4: Model diagnostics (with 95% CI)

Measure	Apparent Performance ¹	Test Performance ²	Average Optimism ³	Optimism corrected ⁴
C-Statistic ⁵	0.79 (0.76 to 0.82)	0.80 (0.77 to 0.80)	-0.0123	0.80 (0.77 to 0.83)
Calibration slope	1.00 (0.87 to 1.13)	0.88 (0.76 to 0.99)	0.1216	0.88 (0.75 to 1.01)

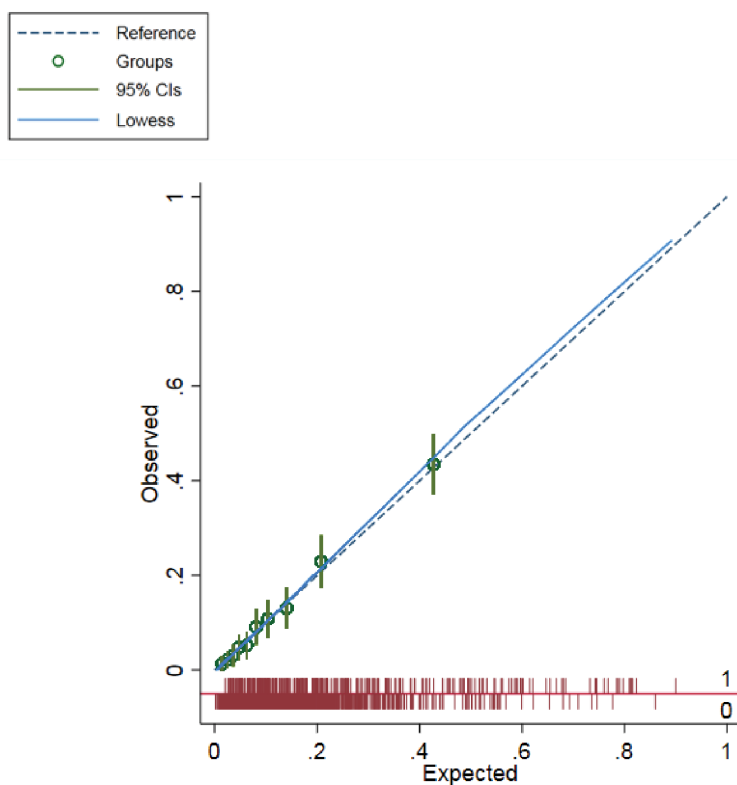
1: Refers to performance estimated from imputation datasets that were used to develop prediction model

2: Determined by developing model in each bootstrapped sample (100 samples with replacement), calculating performance (bootstrap performance), and applying bootstrap model in original imputed dataset.

3: Average difference between model performance in bootstrap data and original imputation data

4: Subtracting optimism from apparent performance

5: Probability that for any randomly selected pair of patients with diagnosed COPD with and without respiratory hospitalisation, the patient with respiratory hospitalisation had higher predicted risk. A value of 0.5 represents no discrimination and 1.00 represents perfect discrimination.

Figure 1: Assessing calibration in original data of the prediction of respiratory hospital admissions within 2 years

Red lines indicate individual respiratory admission events

Table S1: Final multivariable model for respiratory hospitalisation risk for participants with chronic obstructive pulmonary disease from cohort entry until 01/04/2016

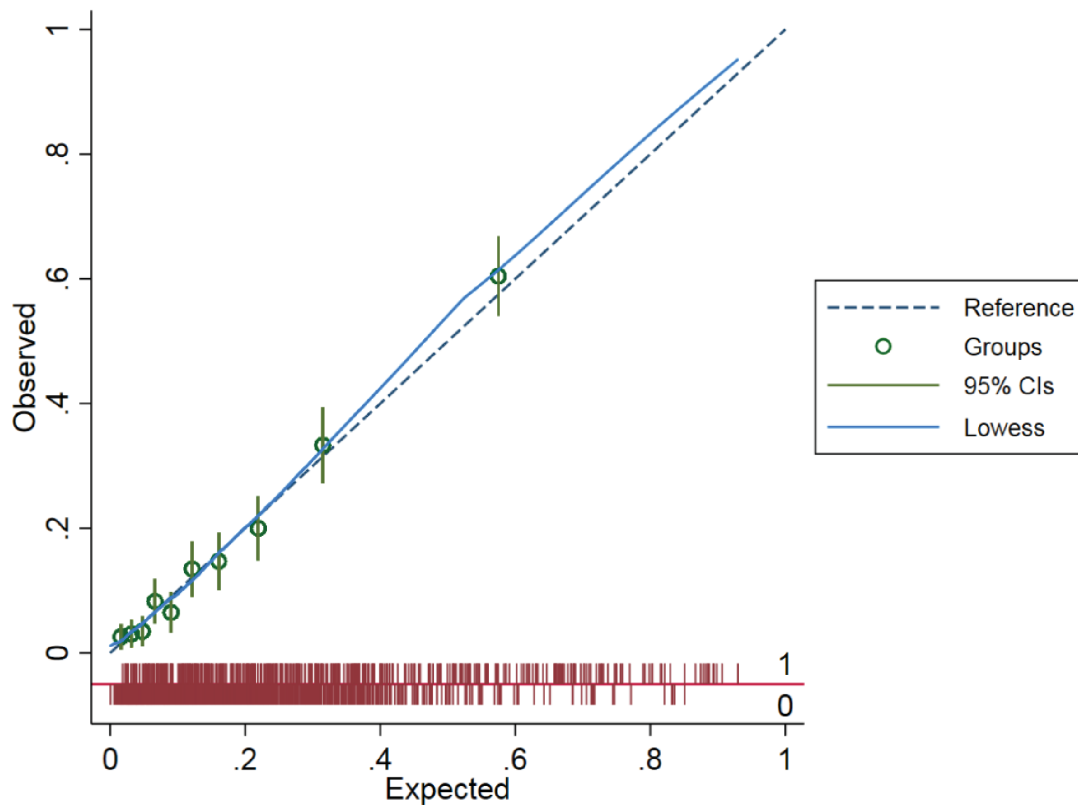
Variable	OR (95%CI)	β coefficients
Obstruction, FEV1/h2	0.086 (0.047 - 0.158)	-2.45280977
Obstruction, FEV1Q	0.997 (0.993 - 1.000)	-0.00326171
Disease specific HRQL Categories	1.044 (1.028 - 1.060)	0.04280823
Gender (Male)	1.483 (1.170 - 1.878)	0.3938612
Previous 12 month respiratory hospitalisation	4.133 (2.732 - 6.252)	1.41900155
Antibiotic/Steroid use	1.282 (1.013 - 1.624)	0.24877863
Bronchial Hyper-responsiveness	0.596 (0.300 - 1.184)	-0.51735871
Diabetes	1.718 (1.269 - 2.324)	0.54087298
Heart Failure	1.403 (0.960 - 2.049)	0.33826103
None-smoker	Reference	-
Current Smoker	2.153 (1.320 - 3.511)	0.76692595
Ex Smoker	1.885 (1.201 - 2.958)	0.63383119
Fractional polynomial transformed		
(bmi/10) ²	-	-0.77622761
(bmi/10) ² x ln(bmi/10)	-	0.44991177
Age/10	-	-6.68969089
Age/10 x ln(Age/10)	-	2.37664856
Constant	-	14.5633

Table S2: Model diagnostics (with 95% CI)

Measure	Apparent Performance ¹	Test Performance ²	Average Optimism ³	Optimism corrected ⁴
C-Statistic _s	0.80 (0.78 to 0.83)	0.80 (0.79 to 0.81)	0.0007	0.80 (0.78 to 0.83)
Calibration slope	1.00 (0.88 to 1.11)	0.88 (0.78 to 0.99)	0.122	0.88 (0.76 to 0.99)

- 1: Refers to performance estimated from imputation datasets that were used to develop prediction model
- 2: Determined by developing model in each bootstrapped sample (100 samples with replacement), calculating performance (bootstrap performance), and applying bootstrap model in original imputed dataset.
- 3: Average difference between model performance in bootstrap data and original imputation data
- 4: Subtracting optimism from apparent performance
- 5: Probability that for any randomly selected pair of patients with diagnosed COPD with and without respiratory hospitalisation, the patient with respiratory hospitalisation had higher predicted risk. A value of 0.5 represents no discrimination and 1.00 represents perfect discrimination.

Figure S1: Assessing calibration in original data for respiratory hospitalisation over full study period



Red lines indicate individual respiratory admission events

APPENDIX 1

List of ICD10 codes used to define respiratory hospital admissions

J00-06, J09-18, J20-22, J39.3, J39.8, J39.9, J40-47, J60-70, J80-86, J90-98, R05, R06.0, R06.2, R06.5, R09.2, R09.3

EME
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HTA
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PHR

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