



# Management of chronic obstructive pulmonary disease in India: a systematic review

Ailsa J McKay<sup>1</sup> • Mahesh PA<sup>2</sup> • Raju KK Patel<sup>1</sup> • Azeem Majeed<sup>3</sup>

<sup>1</sup>Imperial College School of Medicine, Imperial College London, London, UK

<sup>2</sup>Department of Respiratory Medicine, JSS Medical College, Mysore, Karnataka, India

<sup>3</sup>Department of Public Health and Primary Care, Imperial College London, London, UK

Correspondence to: Dr Ailsa McKay. Email: ailsa.mckay08@imperial.ac.uk

## DECLARATIONS

### Competing interests

None

### Funding

This review forms part of a project for which funding was awarded to AJM by the Association of Commonwealth Universities and the Royal College of Physicians of London. The funders played no role in study design, data collection or interpretation, the writing or dissemination of this review. The Department of Primary Care & Public Health at Imperial College London is grateful for support from the NIHR Collaboration for Leadership in Applied Health Research & Care (CLAHRC) Scheme, the NIHR Biomedical

## Summary

**Objectives** Chronic diseases are fast becoming the largest health burden in India. Despite this, their management in India has not been well studied. We aimed to systematically review the nature and efficacy of current management strategies for chronic obstructive pulmonary disease (COPD) in India.

**Methods** We used database searches (MEDLINE, EMBASE, IndMED, CENTRAL and CINAHL), journal hand-searches, scanning of reference lists and contact with experts to identify studies for systematic review. We did not review management strategies aimed at chronic diseases more generally, nor management of acute exacerbations. Due to the heterogeneity of reviewed studies, meta-analysis was not appropriate. Thus, narrative methods were used.

**Setting** India

**Participants** All adult populations resident in India

**Main outcome measures** 1. Trialled interventions and outcomes  
2. Extent and efficacy of current management strategies  
3. Above outcomes by subgroup

**Results** We found information regarding current management – particularly regarding the implementation of national guidelines and primary prevention – to be minimal. This led to difficulty in interpreting studies of management strategies, which were varied and generally of positive effect. Data regarding current management outcomes were very few.

**Conclusions** The current understanding of management strategies for COPD in India is limited due to a lack of published data. Determination of the extent of current use of management guidelines, availability and use of treatment, and current primary prevention strategies would be useful. This would also provide evidence on which to interpret existing and future studies of management outcomes and novel interventions.

**Key words:** COPD, chronic disease management

Research Centre  
scheme and the  
Imperial Centre for  
Patient Safety and  
Service Quality

#### Ethical approval

As a review of  
existing data, ethical  
approval was not  
required

#### Guarantor

AJM

#### Contributorship

AJM, MPA and AM  
contributed to study  
design. Data were  
collected and  
analysed by AJM  
and RKKP. AJM,  
MPA and AM  
drafted/revised the  
article. The final  
version has been  
approved by all  
authors

#### Acknowledgements

The authors would  
like to thank Lambert  
Felix, who kindly  
performed the  
CINAHL database  
search

## Introduction

The recent and rapid increase in the prevalence of chronic disease is a global concern, but a particular threat to health systems in developing countries. Rising prevalence of chronic diseases could destabilize not only health systems but entire state economies, which has been acknowledged at the highest levels.<sup>1,2</sup>

Chronic obstructive pulmonary disease (COPD) is one of several diseases contributing to the rise of chronic illnesses. Typically it results from accumulated environmental exposure to particular irritants – the best established links being with smoking, and domestic and outdoor pollution. More recently, interactions between tuberculosis, HIV and smoking have become of increasingly greater concern, as aetiological factors, as cases of HIV, tuberculosis and co-infection have risen.<sup>3</sup>

That COPD is largely environmentally-driven, and thus potentially preventable, is particularly important in the face of unfavourable epidemiological reports. COPD accounted for 5% of deaths globally in 2005, with most of these occurring in low- and middle-income countries,<sup>4</sup> and it is predicted to become the third leading cause of death by 2030.<sup>5</sup> The outlook may become even worse if COPD associated with HIV/tuberculosis-related lung disease proves to be relatively resistant to existing treatments, and if issues associated with poor nutrition (which appears to be associated with poorer outcomes) cannot be resolved.<sup>6</sup> As a chronic disease, COPD also accrues vast numbers of disability-adjusted life years (DALYs). Most of these arise in the World Bank's 'South Asia' and 'East Asia' regions.<sup>7</sup>

India suffers among the highest number of DALYs due to COPD.<sup>8</sup> The prevalence of COPD in India is not well understood, but we recently suggested the best existing estimates for chronic bronchitis (a commonly used proxy) indicate that prevalence is between 6.5% and 7.7% in the adult population – although it is unlikely that this estimate would apply to all Indian subpopulations.<sup>9</sup> World Health Organization (WHO)-Government of India COPD management guidelines were produced in 2003,<sup>7</sup> but the extent of their implementation, and effect, are unknown. Outcomes have not obviously been reviewed or audited, and the guidance was largely drawn

from similar international documents – based on outcomes from trialled interventions in populations from other, generally more developed countries.

## Review aims

We aimed to review the current quality of management of COPD in India by addressing the following questions:

- (1) How is COPD in India currently managed?
- (2) How effective is the current management of COPD in India?

## Methods

The Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (Cochrane Library), Database of Promoting Health Effectiveness Reviews (Evidence for Policy and Practice Information Centre) and Medline (via PubMed) were searched before conducting the review, on 30 October 2010, to ensure that there were no recent or ongoing reviews in the subject area. The review was then conducted according to the relevant aspects of the PRISMA guidance<sup>10</sup> and the guidance of the Centre for Reviews and Dissemination, York.<sup>11</sup>

Following scoping searches a review protocol was developed describing the search strategy and methods for data collection and analysis. The review questions above were deconstructed to identify PICOS elements used to generate search terms (see Table 1). The search strategy was trialled before use to determine that existing related well-cited articles would be returned, and adaptations made where necessary.

## Search

The PICOS identifiers and related terms (Table 1) were used to search the Medline (via PubMed) and Embase (via Ovid) databases on 1 August 2011 (updated 22 December 2011), the IndMED database on 15 July 2012, Cochrane Central Register of Controlled Trials on 16 July 2012, and the CINAHL database on 24 July 2012. No restrictions were placed on language of publication, study

**Table 1****PICOS identifiers from research questions ('key terms') and database – and thesaurus-derived alternatives ('additional terms') used to generate database searches**

	<i>P</i>	<i>I</i>	<i>C</i>	<i>O</i>	<i>S</i>
Key terms	All populations resident in India	N/a	N/a	COPD	N/a
Additional terms generated	India	N/a	N/a	COPD, COAD, chronic obstructive pulmonary disease, chronic obstructive airway disease, chronic obstructive airways disease, chronic obstructive lung disease, chronic bronchitis, 'bronchitis, chronic', emphysema*, chronic airflow obstruction*, 'airflow obstruction*, chronic'	N/a

Stars indicate where all database terms based on the attached stem were included. Terms within each column were distinguished using the OR function, and the terms in different columns combined using the AND function

design, publication type or publication status. Only studies published since 1980 were included, as our interest was in the recent situation, and earlier publications were also relatively few and difficult to access.

In addition, the available online contents (from 1980 onwards) of the journals *Lung India* and *Indian Journal of Chest Diseases and Allied Sciences* were hand-searched on 19 August 2011. Reference lists of included papers were scanned, as well as the references of relevant review articles/editorials identified in the search. Finally, we contacted experts in the field with the aim of identifying any additional or unpublished data. We did not include unpublished results available on trial databases as we felt unable to assess the data in a sufficiently useful manner, due to lack of information such as location and dates of study, methodology, length of follow-up and general analytical approach. Many of the trials recruited from multiple countries and data for India alone were not available. We also felt unable to interpret data regarding adverse events sufficiently well.

### Selection

Inclusion/exclusion criteria for the results of the search are listed in Table 2.

Two subsets of results pertaining to Question 1 were acquired – studies of primary and secondary

prevention. The number of primary prevention studies returned was limited and we included them even though the interventions were not conceived to target COPD alone. In the series of secondary prevention studies returned, we made no exclusions based on intervention type, so long as the study pertained to the management of chronic, stable COPD, rather than acute events. Indeed, observation of the types of intervention pursued was of interest in itself. Similarly, regarding Question 2, we included studies of all measured outcomes, other than those relating to acute exacerbations alone.

To determine study eligibility, the titles and abstracts of all papers returned from the search were screened by one reviewer. The studies accepted at this point were reviewed fully, and progressed either to data extraction or exclusion. Those excluded were: reviews/editorials without additional analysis, studies wherein data were not COPD-specific, where populations were not representative of the general population, interventions were of acute management and/or studies were without actual trialled intervention, were not relevant, or not available (see Figure 1).

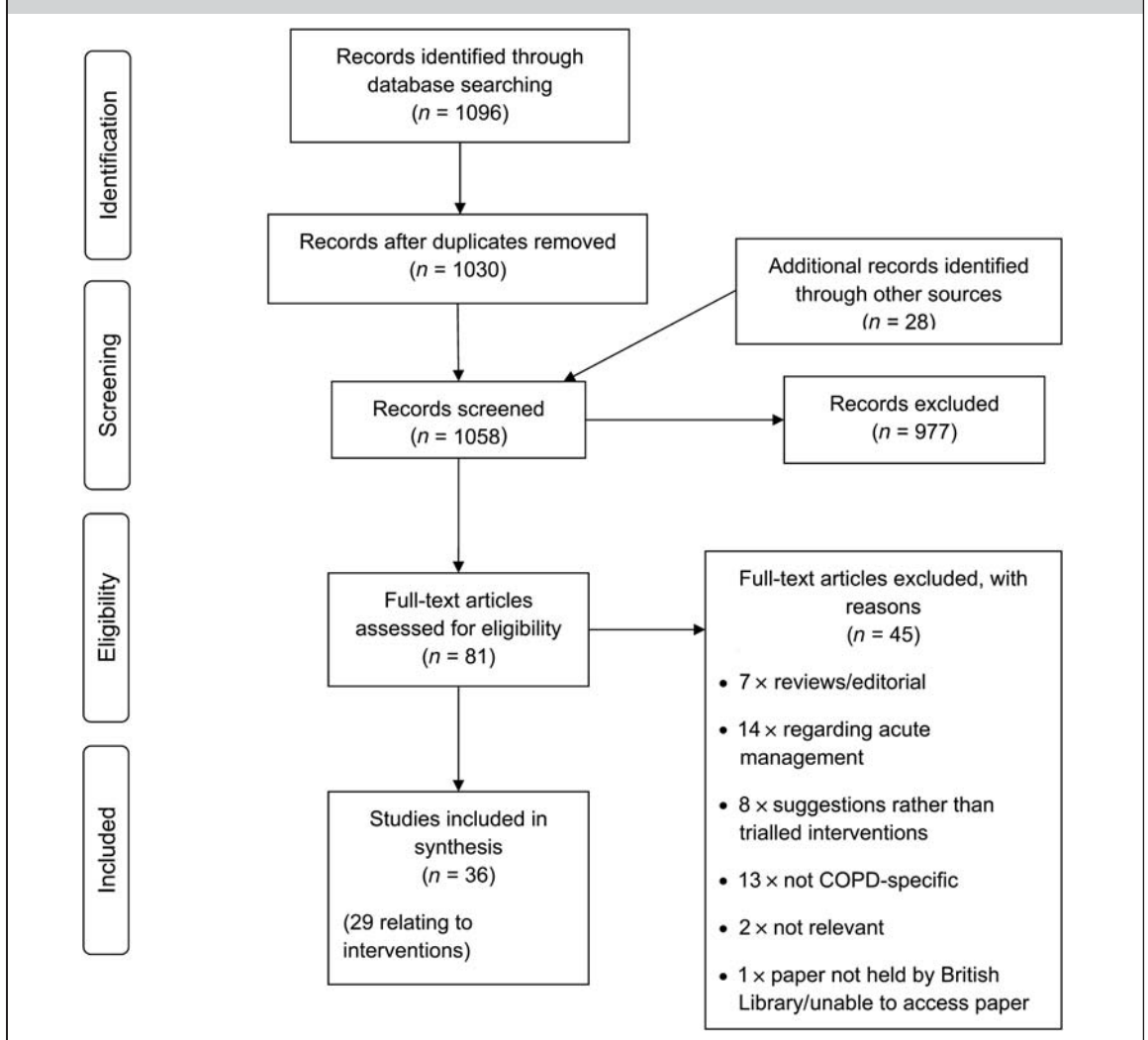
### Data extraction

Data extraction was performed using two proformas – one for extraction of basic study data, one for quality assessment. The basic study data

**Table 2**  
Inclusion/exclusion criteria

Included	Excluded
All categories (mild–very severe) of COPD Management of chronic, stable COPD	Management strategies relevant to management of chronic diseases generally, but not COPD specifically Management strategies applicable to management of acute exacerbations of COPD Review articles without novel synthesis
All outcomes – including those objectively and subjectively defined, and process and clinical measures	
COPD, chronic obstructive pulmonary disease	

**Figure 1**  
Flow chart demonstrating handling of papers returned by Searches 1 and 2



**Box 1****Data extraction and quality assessment checklists**

The numbers beside the quality assessment criteria are used to indicate how quality for each criterion has been rated, in Tables 3–5.

*General data extraction*

- Study dates (or publication date if not available)
- Study design
- Type of report
- Number of participants (enrolled, excluded and lost to follow-up)
- Participant characteristics (including age, sex, smoking status, exposure to domestic fuels and socioeconomic status, where available)
- Study setting (location and urban or rural)
- Definition of diagnosis used
- Measurement/assessment tool
- Outcomes (including subgroup data for age, sex, urban/rural residence, smoking status and domestic fuel exposure where available)

*Quality assessment checklist*

1. Type of report
2. Clear aims/objectives
3. Clear and appropriate methods, including sampling/recruitment (4), inclusion/exclusion criteria (5) and data collection
6. Appropriate and rigorous analysis
7. Outcomes not reported or additional outcomes reported
8. Risk of bias in selection
9. Risk of bias in measurement and outcomes
10. Limitations discussed
11. Funding information and information regarding conflicts of interest

proforma was a modified version of the checklist recommended by the Centre for Reviews and Dissemination, York.<sup>11</sup> Our quality checklist has been used previously<sup>9</sup> and includes the 'component ratings' of the Effective Public Health Practice Project Quality Assessment Tool<sup>12</sup> and the bias assessment as recommended in the Cochrane Handbook.<sup>13</sup> It was used for all study types, with items omitted where not relevant. The proformas were tested on a subset of the papers, and iterations made, before being used for final data collection. The broad headings under which information was recorded for each study are listed in Box 1.

One reviewer carried out the data extraction for basic study data. The results were checked by a second reviewer and any concerns remedied by re-checking to reach a consensus decision. Two reviewers independently performed the extraction of quality data, before the results were collated. Inconsistencies were resolved as above.

**Quality assessment**

The extracted quality data were used to grade each aspect of the assessment as 'good', 'poor' or 'non-assessable'. Again this rating was independently carried out by two reviewers. Disagreements

were resolved by discussion and consensus decision. Where the combination of the number of 'poor/non-assessable' ratings and main reasons for concern were deemed sufficient to question the reliability of the study, the study was excluded from a secondary analysis (see below).

**Data synthesis**

As anticipated on preliminary searching, study designs were too heterogeneous to allow useful meta-analysis. Thus, a narrative approach was used. The data were summarized in tables, and analysed twice (before and after exclusion of studies where quality was of concern).

We aimed to assess each set of studies with regard to:

- Number of studies and time-trends in production and quality.

We wanted to examine the management intervention studies to determine:

- Types of intervention trialled and levels of success;

- Any peculiarities of intervention effect by subgroup (age, sex, urban/rural location, smoking status and exposure to domestic fuels).

And we aimed to examine the management outcome studies to determine:

- Outcome measures used;
- Extent and efficacy of current management strategies;
- Any differences in outcomes by subgroup.

Proposals were formed based on general initial analysis outcomes, and inconsistencies examined. Finally, comparisons between results of the analyses were made before and after studies with quality concerns were excluded. Where data were insufficient to allow narrative synthesis, display and discussion of the data was used.

## Results

The search produced 1096 papers for review. Figure 1 displays the handling of the search results.

The data extracted from each of the studies are summarized by question theme in Table 3 (primary prevention management interventions), Table 4 (secondary prevention management interventions) and Table 5 (management outcomes). The data excluded from the second analyses (due to quality concerns – see Methods), are italicized, and the main quality concerns noted.

### Management I – interventions

Twenty-nine studies of interventions were identified – two relating to primary prevention and 27 to secondary prevention. Other than two studies published in the 1980s, and three in the 1990s, all had been published within the last decade. Generally, more recent studies had higher-quality scores.

Regarding the two primary prevention studies – neither was a clear, trialled and audited study, and neither was conceived to address COPD alone. Although one<sup>14</sup> scored well on quality assessment, it was a theoretical study, with the associated uncertainties. The second<sup>15</sup> was a

conference abstract, with poor-quality scores, and difficulty in interpretation limited its use.

The 27 studies investigating secondary prevention interventions showed much variety in intervention type, study setting and outcome measures. There were 17 pharmacological interventions, three pulmonary rehabilitation interventions, five others involving exercise training, one trial of influenza vaccination and one study of the World Health Organisation-Government of India guidelines. All were assessed using intermediate clinical outcome measures. The guidelines and vaccination interventions were assessed using a quality-of-life questionnaire and exacerbation frequency, respectively. The other categories of intervention were each assessed by a combination of spirometry, exercise capacity and other physical measures, as well as quality-of-life scores.

Of the trialled interventions, only six had negative outcomes,<sup>21,25,27,32,35</sup> and of those with positive outcomes, only the implementation of the WHO-Government of India guidelines was potentially still ongoing. Indeed, in several cases the follow-up was so limited that the relevance of the intervention was unclear.<sup>21,23,35,38,41</sup> The clinical relevance of the changes rendered by some studies<sup>20,23,32,33,42</sup> was also unclear.

Discounting these studies of questionable relevance, and those with quality concerns, only 10 studies of relatively high usability were left.<sup>16,18,19,24,26,29,30,34,37,40</sup> Notably, all of these studies had positive outcomes, but they were of varied intervention type (5 pharmacological, 2 pulmonary rehabilitation, 2 other exercise interventions and 1 regarding vaccines), and each was confined to a particular geographical area. Their generalizability was therefore limited. Four of the studies (of bronchodilator use and pulmonary rehabilitation) were of interventions already recommended in Indian guidelines. Although subgroup outcomes are of interest with regard to disease patterns and targeting interventions, the low number and heterogeneity of studies did not permit such investigation.

### Management II – outcomes

Seven studies relating to outcomes were identified – two from the 1980s, one from the 1990s and four more recent. Again fewer quality concerns were



**Table 3**  
**Studies relating to primary prevention strategies for chronic obstructive pulmonary disease in India**

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Units of assessment, definitions and follow-up	Outcomes	Quality
14	2010–2020; modelling study	n/a – model based on all India	Intervention: 10 year programme to introduce 150 million low-emissions household cookstoves in India Methods: similar to WHO's Comparative Risk Assessment exercise – applied to assess effect on health	Units of assessment: deaths and DALYs avoided	Deaths from COPD avoided in 2020: 28.2% Number of deaths avoided 2010–2020: $1.27 \times 10^6$ DALYs avoided 2010–2020: 9%	G: 1, 2, 3, 6, 7, 10, 11 P: N: (NB 4, 5, 8 and 9 not listed due to nature of study)
15	'from May 2007' (P2009); quasi-experimental study; '11 villages, rural India'	n = 493; 14–24 years; 32% COPD and respiratory disorders, 12% tuberculosis	Intervention: Tobacco de-addiction guidance/counselling offered by NGO Methods: Counselling effect monitored for four months (20 follow-up sessions conducted during course of study)	Unit of assessment: discontinuation of tobacco use; reasons for starting tobacco use	431 'showed positive attitude towards quitting tobacco use'; 410 discontinued tobacco use; 21 abstained for short-period, but re-started Of 431 with positive response: 84% started using tobacco due to peer pressure, 11% to imitate tobacco advertising on media/films/TV	G: P: 1, 2, 3, 7, 10 N: 4, 5, 6, 8, 9, 11 Main concerns: abstract therefore limited information; objectives and methods particularly unclear

Reviewed studies regarding primary prevention strategies relevant to chronic obstructive pulmonary disease (COPD). Study entered in italics of quality concern (see Methods), with the main reasons for concern noted in the 'Quality' column. The numbers following the different quality 'levels' (G, P, N) indicate the aspect of quality assessment (see Box 1), rated as good (G), poor (P) or not-assessable (N)  
 WHO, World Health Organization; DALYs, disability adjusted life years

**Table 4**  
**Studies relating to secondary prevention strategies for chronic obstructive pulmonary disease in India**

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
16	P2010; RCT; Jaipur	n = 33 (15 experimental, 18 control); mean age: 60.7 (SD 8.5) in sildenafil arm; 63.6 (SD 6.7) in placebo arm; patients with severe/very severe COPD by GOLD classification, > 20 pack year history and pulmonary artery systolic P > 40 mmHg	Intervention: oral sildenafil TDS Methods: double blind, randomized, placebo-controlled; 12-week follow-up	6MWD; pulmonary arterial pressure	Sildenafil group: 6MWD significantly higher at one and three months; pulmonary arterial pressure significantly lower at three months Placebo group: no change in either measure	G: 1, 2, 3, 5, 6, 9 P: 7, 10 N: 4, 8, 11 Main concerns: drug and placebo supplied by drug company, but extent of further input not mentioned
17	P2011; quasi-experimental study; Dehradun	n = 20 (10 experimental, 10 control); 100% men; 'severe' COPD	Intervention: domiciliary pulmonary rehabilitation programme Methods: follow-up six months	CCQ; 6MWD; spirometry	Significant differences between groups in CCQ scores and 6MWD from fourth month onwards (higher in intervention group); no significant difference in spirometry	G: 1, 2, 5, 6, 7, 10 P: 3, 4, 8, 11 Main concerns: non-randomized – only willing participants in intervention group
18	2009–2010; parallel group study; Jammagar	n = 61; moderate-severe COPD Experimental group: mean age + SD: 58.39 + 8.58 years Control group: mean age + SD: 56.53 + 11.29 years	Intervention: doxycycline daily Methods: randomized, single-blind; four weeks follow-up	Spirometry, CRP, MRC dyspnoea scale	Intervention group: significant increase in FEV1 and FVC during study period; significantly greater improvement in spirometric parameters and reduction in baseline CRP cf. control group, no change in dyspnoea score Control group: No change in lung function parameters or dyspnoea score	G: 1, 2, 4, 6, 7, 10 P: N: 3, 5, 8, 9, 11
19	P2010; RCT; Mangalore	n = 30 (10 in each group); 100% men; 45–75 years; clinically stable	Intervention: upper-limb training, lower-limb training or upper and lower-limb training Methods: no controls; four-week follow-up	Unsupported upper-limb endurance test; 6MWD CRQ	Compare to pretraining: Upper limb training: improved endurance test and CRQ; Lower limb training: improved 6MWD and CRQ; combined training: improved all outcomes	G: 1, 5, 6, 7, 11 P: 2, 3, 4, 10 N: 8, 9 Main concern: lack of information regarding training programme/ intervention

(Continued)



Table 4  
Continued

Ref. Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
20 P2010; RCT; Chidambaram	n = 16 (7 experimental, 9 controls); 40–68 years	Intervention: unsupported arm exercises 3x per week Methods: randomized; 1 month follow-up	12MWD, spirometry	Significant improvement in FVC values in both groups, no change in FEV1 in either group 'Significant' change in 12MWD – NB direction of change unclear, one 'significant' value 'P < 0.053'	G: 1, 2 P: 6, 7, 9, 10 N: 3, 4, 5, 8, 11 Main concerns: small n-number, little information re methods, data not reported in results (only results of tests) therefore size/relevance of differences unclear, significance level unclear, conclusions not in line with results
21 P2007; RCT; Mumbai/Pune	n = 19; 89.5% men; mean age 59.15 (SD 7.98) years; stable moderate-severe COPD by GOLD criteria	Intervention: pMDI Methods: randomized, double-blind, placebo-controlled, cross-over study; single doses of tiotropium via pMDI plus spacer; and by DPI, and placebo administered on three separate days at least four days apart; 24 hour follow-up	Spirometry, body plethysmography	FEV1, FVC and IC significantly higher in MDI and DPI cf placebo groups No differences between outcomes in MDI and DPI groups	G: 1, 2, 3, 5, 6, 7, 9, 11 P: 10 N: 4, 8
22 2006–2007; RCT; Chandigarh	n = 74 (42 experimental; 32 control); patients with mild COPD excluded Experimental group: 95.2% men; 36–80 (mean 60) years; 95.2% smokers Control group: 90.6% men; 35–83 (mean 61) years; 90.6% smokers	Intervention: WHO-Government of India COPD guidelines Methods: controls received 'conventional' treatment; six months follow-up	SGRQ: change of > 4 units considered significant	Follow-up scores significantly higher than baseline in both groups, and significantly higher postintervention cf. post control treatment	G: 1, 2, 4, 5, 10, 11 P: 3, 6, 7, 9 N: 8 Main concern: some elements of methodology – including recruitment and analysis – not well described; not all outcomes reported; potential differences in disease phenotype between groups; control arm treatment not well described and administered by different individuals; high potential for bias

(Continued)

**Table 4**  
Continued

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
23	P2006; RCT; Delhi	n = 44; 100% men; 38–78 years; stable patients; eight mild, 19 moderate and 17 severe (by GOLD guidelines)	Intervention: single doses of formoterol, ipratropium bromide or placebo Methods: randomized, double blind, crossover, placebo-controlled; treatments administered on three consecutive days in random order, follow-up one hour	Spirometry, static lung volumes, heart rate, blood pressure and perceived dyspnoea assessment	Formoterol and ipratropium led to similar significant increases in FEV1 and FVC scores, improved static lung volumes and dyspnoea scores Placebo did not lead to significant improvements in any outcome	G: 1, 2, 3, 5, 6, 7, 9, 10 P: N: 4, 8, 11
24	P2006; RCT; Chennai	n = 105 (32 drug arm, 39 plant arm, 34 placebo arm); 100% men; 35–85 years; 'moderate' and stable disease	Intervention: DCBT1234-Lung KR (plant extract), drug combination (salbutamol, theophylline and bromhexine) or placebo Methods: randomized, placebo controlled study; six-month follow-up	Spirometry, ABG analysis, COPD symptoms	DCBT1234-Lung KR led to significant improvement in FEV1 and PaO2; other treatments did not DCBT1234-Lung KR patients showed significant improvement in all clinical symptoms studies; drug treatment did not improve dyspnoea or disability	G: 1, 2, 3, 5, 6, 7, 9 P: 10, 11 N: 4, 8 Main concern: involvement of 'Dalmia Brothers Private Limited' not delineated
25	P2006; RCT; Delhi	n = 60 (31 experimental; 29 controls); 100% men; ex-smokers Experimental group: mean age: 26.94 (SD 8.79) years; duration of disease: 5.00 (SD 5.06) years Control group: mean age: 62.72 (SD 9.51) years; duration of disease: 9.52 (SD 4.36) years	Intervention: oral prednisolone Methods: randomized study; seven days treatment, assessment on day 8	Spirometry, bronchodilator responsiveness	No response to intervention found; no differences between groups found	G: 1, 2, 3, 6, 7, 10 P: 8, 9 N: 4, 5, 11 Main concerns: significantly different mean age and duration of disease between intervention and control groups; not blinded, no placebo
26	P2006; RCT; Kanpur	n = 48 (24 per group) Intervention group: mean age 53.3 (SD 2.9) years; 78% men Control group: 51.1 years; 91% men	Intervention: Pranayama yoga techniques Methods: randomized, single-blind; follow-up three months	Spirometry, ABG, 6MWD, SGRQ	Intervention group: longer 6MWD, higher PEF and lower SGRQ scores after training; no significant effect in other parameters Control group: no significant changes over study period	G: 1, 2, 4, 5, 6, 7, 9 P: 10 N: 3, 8, 11

(Continued)

**Table 4**  
**Continued**

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
27	P2006; parallel group study; Delhi	n = 32 (16 per group); severe COPD Tiotropium group: mean age 58.8 (SD 9.33) years Ipratropium group: 59.3 (SD 9.26) years	Intervention: Daily tiotropium bromide or ipratropium bromide Methods: non-randomized, parallel group study (sequential design viz controls); six-week follow-up (plus 6 weeks preintervention)	Spirometry, 6MWD, perceived dyspnoea, CRQ	No obvious effect of either treatment (although analysis unclear – see column 7)	G: 1, 2, 4 P: 5, 6, 9, 10 N: 3, 7, 8, 11 Main concerns: recruitment not detailed, non-randomized, multiple comparisons, comparisons (and therefore outcomes) unclear; (potential) control period not analysed as such
28	2005–2006; design unclear; Delhi	n = 40 (20 experimental, 20 control); no information re participants reported	Intervention: 'Sharbat-e-Unsul Murakkab', dose unclear Methods: single blind, placebo-controlled; follow-up 21 days	'History', PEFR, haemogram, eosinophil count, liver function tests, renal tests, sputum culture	'Improvement' in cough, sleep disturbance, 'hypnotic effect', sputum purulence sputum volume, sputum viscosity, dyspnoea, rhonchi and PEFR in experimental, but not control, subjects	G: 1 P: 2, 6, 7, 9, 10 N: 3, 4, 5, 8, 11 Main comments: study design (randomization) unclear, no information re participants, dose of drug not reported, outcome measures not defined, data collection methods unclear, non-significant results reported as significant, conclusions not in line with results
29	2004–2006; quasi-experimental study; Delhi	n = 87; 100% men; mean age 64.8 years (SD 8.5); 28.7% smokers, 54% ex-smokers; never before received influenza vaccination	Intervention: influenza vaccination Methods: patients treated according to GOLD guidelines and followed up for one year pre- and postvaccination	Exacerbations (diagnosis = increasing shortness of breath and increase in amount or purulence of sputum)	Exacerbations due to 'natural infections' significantly lower post-vaccination (effectiveness = 60%, 60% and 75% in mild, moderate and severe COPD, respectively); outpatient and hospital admission lower postvaccination	G: 1, 2, 3, 5, 6, 7 P: 8, 9, 10 N: 4, 11 Main concern: sequential study design
30	P2005; pilot study, unclear if randomized; Delhi	n = 20; current smokers not willing to give up smoking excluded; stable patients with moderate to severe COPD attending outpatient department of tertiary care centre; little other information reported	Intervention: home-based pulmonary rehabilitation programme (including: education, exercise training, nutritional support, psychosocial support Methods: six weeks follow-up	Spirometry; perceived dyspnoea assessment; 6MWD; MIP; CRQ	Intervention produced significant improvements in 6MWD, dyspnoea score, and all four domains of CRQ (dyspnoea, emotional, fatigue and mastery scores) cf. baseline, and no significant changes in MIP or spirometry Results of control study not clearly reported	G: 1, 2, 3, 5, 7 P: 6, 10 N: 4, 8, 9, 11

(Continued)

**Table 4**  
Continued

Ref. Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
31 2004–2005; RCT; Aligarh	n = 100 (50 experimental; 50 control); moderate-severe COPD Experimental group: 76% men, mean age 62.6 (SD 6.2) years; control group: 80% men, mean age 60.1 (SD 7.3) years	Intervention: 600 mg oral N-acetylcysteine daily for four months Methods: randomized, single-blind, placebo-controlled; one year follow-up	Spirometry, exacerbation frequency	Fewer exacerbations in intervention group Spirometry values increased more in intervention cf control group (although no clear increase within either group)	G: 1, 2, 4 P: 10 N: 3, 5, 6, 7, 8, 9, 11 Main concerns: recruitment, data collection and analysis not well-described
32 2002 – 2004; RCT; Delhi	n = 24 (10 experimental; 14 control); 100% men Experimental group: mean age 54.86 (SD 7.13) years; control group: mean age: 60.10 (SD 1.16) years	Intervention: vitamin E supplementation Methods: randomized, single-blind, placebo-controlled; eight-week follow-up	Spirometry; 'clinical assessment'; 'several biochemical parameters of oxidant-antioxidant status'	Similar degree of lung function and clinical improvement (significant) in both groups Experimental group: higher plasma sulphhydryls and red cell catalase cf. control group Plasma nitrates and nitrites decreased in control, but not experimental, group	G: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 P: N:
33 P2003; observational study; Delhi	n = 30 (30 COPD patients (15 experimental); > 35 years; 80% men	Intervention: 400 IU vitamin E daily Methods: randomized, control and blinding unclear; 12-week follow-up	'Clinical examination', spirometry, plasma malondialdehyde, alpha-tocopherol and red cell superoxide dismutase	Experimental group: MDA levels fell over study period; no other changes in any parameters over study period	G: 1, 2, 4 P: 6, 7, 10 N: 3, 5, 8, 9, 11 Main concerns: Recruitment unclear; no control (results reported) for period of vitamin E supplementation; only half of COPD group received vitamin E
34 P2003; RCT; Jaipur	n = 40 (20 experimental, 20 control); 80% men; 48–75 years (mean age 59.37 (SD 6.4 years)); severe COPD; never involved in pulmonary rehabilitation programme and smoking cessation for > 2 months	Intervention: domiciliary pulmonary rehabilitation programme Methods: four-week follow-up	6MWD; FEV1; CRQ	Significant improvement in 6MWD and CRQ scores in experimental cf. control group No significant change in FEV1 in either group	G: 1, 2, 3, 5, 6, 7, 9 P: 5, 10 N: 4, 8, 11

(Continued)

**Table 4**  
**Continued**

Ref. Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
35 P2003; RCT; Delhi	n = 8; 100% men; mean age 52 years	Intervention: Salbutamol, ipratropium bromide or beclomethasone dipropionate Methods: randomized, cross-over, placebo-controlled; each drug/placebo given randomly on four separate days; 24-hour follow-up	Radioaerosol inhalation lung cinescintigraphy/mucociliary clearance	No significant clearance with any drug, and no difference cf. placebo	G: 1, 2, 5, 6, 7 P: 3, 10 N: 4, 8, 9, 11 Main concerns: very low n-number
36 P2002; RCT; Delhi	n = 33 (17 experimental, 16 control); 100% men; moderate/severe COPD (BTS criteria) Experimental group: mean age 59.06 (SD 10.57) years; mean smoking history: 39.96 (SD32.2) years Control group: mean age 56.81 (SD 12.49) years; mean smoking history: 56.56 (SD 52.3) years	Intervention: salmeterol Methods: double-blind, randomized, placebo controlled; eight-week follow-up	Spirometry; 6MWT; quality-of-life questionnaire; perceived dyspnoea assessment; patient's self-assessment of symptoms; supplemental use of salbutamol	Significant increase in FEV1 and FVC in salmeterol group, but not placebo group, and significant effect of salmeterol in both measures versus placebo Salmeterol also led to greater improvements quality-of-life questionnaire, dyspnoea assessment, self-assessment of symptoms and salbutamol use 6MWD similar in both groups	G: 1, 2, 3, 5, 6, 7, 9 P: 10 N: 4, 8, 11
37 P2001; quasi-crossover trial; Mysore	n = 30; 100% men; mean age 65 (SD 7.74) years; 'mild-severe'	Intervention: ipratropium or theophylline for one month, the other for second month and combination for third month Methods: followed up every 15 days	Spirometry, quality-of-life questionnaire, functional ability/impairment; perceived dyspnoea	FEV1 and quality-of-life scores were higher than baseline following all three treatments FEV1 and quality-of-life scores were significantly higher following ipratropium cf theophylline treatment, and in the combination - cf single drug - treated groups	G: 1, 2, 6, 7 P: 3, 10 N: 4, 5, 8, 9, 11 Main concern: combination treatment not part of crossover design (administered to all participants in third month)

(Continued)

**Table 4**  
Continued

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
38	P1999; RCT; Aligarh	n = 97 (32 salbutamol, 29 ipratropium and 36 combined group); 'mild-moderate symptoms'; excluded if other chronic disease Salbutamol group: 59% men; mean age 57.1 (SD 11.4) years; 69% smokers Ipratropium group: 62% men; mean age 61.7 (SD 13.7) years; 66% smokers Combination group: 58% men; mean age 58.6 (SD 13.1) years; 67% smokers	Intervention: inhalation of salbutamol, ipratropium bromide or combination Method: salbutamol, ipratropium or both administered; four-hour follow-up	FEV1	No baseline differences Ipratropium significantly higher mean FEV1 cf. salbutamol at 180 and 240 minutes Combination treatment significantly higher mean FEV1 cf salbutamol at 120, 180 and 240 minutes	G: 1, 2, 3, 5 P: 6, 7, 10 N: 4, 8, 9, 11 Main concerns: methods including recruitment, randomization and data analysis unclear; not all outcomes reported
39	P1998; quasi-experimental study; Chandigarh	n = 15; 93% men; mean age 58.9 (SD 11.05) years; volunteer patients	Intervention: yoga therapy Methods: therapy delivered for four weeks	FEV1, PEFR, VC, perceived dyspnoea	Yoga therapy associated with improved perceived dyspnoea, FEV1, PEFR and VC measurements	G: 1, 6, 10 P: 2, 4, 5, 8 N: 3, 7, 9, 11 Main concerns: volunteer patients selection bias; little information regarding methods; relatively high degree of potential bias
40	P1991; parallel group study; Tamil Nadu	n = 45 (15 per group); groups 53 – 60% men; age range: 35–75 years Deriphylline group: mean age 54.5 (SD 12.6) years; 53% men; salbutamol group: 51.3 (SD 9.9) years; 60% men; terbutaline group: 47.0 (SD 5.4) years; 60% men	Intervention: oral deriphylline, salbutamol or terbutaline daily Methods: uncontrolled, parallel group design; follow-up three weeks	PEFR	Significant rise in PEFR in salbutamol and terbutaline groups No change in deriphylline group	G: 1, 2, 4, 5, 6, 7, 9 P: N: 3, 8, 10, 11
41	P1989; quasi-crossover study; Tirupati	n = 10; 100% men; 35–60 years (mean age 48.5 (SD 9.75) years)	Intervention: inhalation of salbutamol or ipratropium bromide or combination Method: salbutamol administered on day 1, ipratropium bromide on day 2, combination on day 3; six-hour follow-up	FEV1, PEFR	Ipratropium significantly more effective than salbutamol and the combination more so with regard to FEV1 and PEFR	G: 1, 7 P: 2, 3, 4, 6, 9, 10 N: 5, 8, 11 Main concerns: low n-number; sequential study design; high risk of bias

(Continued)



**Table 4**  
**Continued**

Ref.	Study dates, design and location	Population size and characteristics	Intervention and methods	Assessment/ follow-up measures	Main outcomes	Quality
42	P1982; RCT; Delhi	n = 75 (25 each group); 100% men Control group: mean age: 49.2 (SD 10.0) years; physiotherapy group: mean age 48.1 (SD 8.44) years; yogasanas group: mean age: 50.6 (SD 12.23) years	Intervention: breathing exercises/ chest physiotherapy or yogasanas Methods: 12-week follow up	Spirometry; ABG analysis; respiratory rate; heart rate	Best maintenance of spirometry in yogasanas group (non-significant) Lower respiratory and heart rates in yogasanas cf. control (intermediate response in physiotherapy group) No ABG change with any treatment	G: 1, 3, 5 P: 2, 6, 7, 8, 10 N: 4, 9, 11 Main concerns: unclear if truly randomized as FEV1/FVC ratios of groups matched; statistical methods and outcomes unclear
<p>Reviewed studies regarding secondary prevention strategies relevant to non-acute management of chronic obstructive pulmonary disease (COPD). Population characteristics are entered as available. Studies of quality concern (see Methods) are entered in italics, with the main concerns being noted in the 'Quality' column. The numbers following the different quality 'levels' (G, P, N) indicate the aspect of quality assessment (see Box 1), rated as good (G), poor (P) or not-assessable (N)</p> <p>RCT, randomized controlled trial; SD, standard deviation; GOLD, = Global Initiative for Chronic Obstructive Lung Disease; WHO, World Health Organization; 6MWD, six-minute walk distance; 12MWD, 12-minute walk distance; CCO, clinical COPD questionnaire; CRQ, chronic respiratory questionnaire (includes 4 domains: dyspnoea, fatigue, emotion and mastery); SGRO, St George's respiratory questionnaire (designed to assess quality of life: impaired health and perceived wellbeing); MIP, maximum inspiratory mouth pressure; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; PEFR, peak expiratory flow rate; ABG, arterial blood gas; CRP, C-reactive protein</p>						

**Table 5**  
**Review of chronic obstructive pulmonary disease management outcomes in India**

Ref.	Study dates and location	Population size and characteristics	Methods and diagnostic and assessment criteria	Outcomes	Quality
43	2008–2009; Bhopal, Madhya Pradesh (urban)	n = 100 (6 stage 1, 32 stage 2, 40 stage 3, 22 stage 4); > 40 years (mean age 61.7 years [SD 9.6]); 100% men; ex-smokers or current smokers; stable patients; excluded if prior diagnosis of depression or chronic systemic diseases	Severity of COPD classified by GOLD criteria Hindi translation (validated) of PHQ-9 used to assess depression	Prevalence of depression: 72% Severity of depression increased with that of COPD	G: 1, 2, 3, 4, 5, 6, 7, 10 P: 9 N: 8, 11
44	2007–2009; Kolkata (urban)	n = 37; severity: GOLD category 3/4; mean age ( $\pm$ SD): 65.32 $\pm$ 9.58 years; men:women ratio 35:2	Diagnosis and severity assessment by GOLD criteria BMD assessed by ultrasound bone densitometer – T-score –1 to –2.5 = osteopaenia, < –2.5 = osteoporosis Uncontrolled study	Prevalence of osteopaenia: 51.35% Prevalence of osteoporosis: 21.62%	G: 1, 2, 5, 10, 11 P: 3, 6, 7 N: 4, 8, 9 Main concerns: limited information regarding methodology, recruitment unclear; no description of analysis methods, but various comparisons performed
45	1994–2004; Delhi (urban)	n = 515; 66% men	All deaths between 1994–2004 analysed using verbal autopsy questionnaire; causes of death recorded using International Classification of Diseases-10 code	COPD second commonest cause of death (11.6% [10.5% men, 13.7% women]) COPD = commonest cause of death in group $\geq$ 65 years	G: 1, 5, 9 P: 2, 3, 6, 7, 10 N: 4, 8, 11 Main concerns: limited information regarding objectives and methodology and no description of analysis methods; scope for bias relatively high
46	1999–2000; Chandigarh City and Panchkula district (urban and rural)	n = 84; > 60 years Mean number of morbidities among the entire sample of elderly people (n = 200; NB. not COPD group alone) was 6.1 (SD 2.9)	'Clinical diagnosis' of COPD (reported illness, clinical examination, cross-checking of medical records and medications); questionnaires for distress (physical and mental) and disability	COPD significantly associated with higher disability and distress scores	G: 1, 2, 3, 4, 5, 6, 7, 8, 10, 11 P: N: 9

(Continued)

Table 5  
Continued

Ref.	Study dates and location	Population size and characteristics	Methods and diagnostic and assessment criteria	Outcomes	Quality
47	P1992; Chandigarh (urban)	n = 150; 92.7% men; 28–78 years; smokers	Questionnaire	66.7% knew disease related to smoking; 88.7% advised by doctor to stop Of patients who had given up smoking; 52.8% due to insistence of doctor, 44% because of their own persistence, and four due to advice by friends; six suggested would resume once symptom-free, 12 undecided	G: 1 P: 2, 3, 6, 7, 10 N: 4, 5, 8, 9, 11 Main concerns: unclear objectives, methodology and analysis; relatively high potential for bias
48	1981–1986; Tamil Nadu (rural)	n = 9946; > 30 years	Questionnaire and PEFR for COPD diagnosis; chest X-rays examined for evidence of cor pulmonale (diagnostic criteria not supplied)	Of 99 patients given chest X-ray, 1 patient had cardiomegaly with clinical evidence of cor pulmonale	G: 1, 2, 11 P: 3, 6, 7, 9, 10 N: 4, 5, 8 Main concerns: some elements of methodology and analysis unclear, information gained from family members where participants unavailable
49	P1982; Jhansi, Uttar Pradesh (rural)	n = 1424; >20 years; 54.4% men 14.8% men never smokers, 73.3% current smokers; 86.0% women never smokers, 12.0% women current smokers	Questionnaire for CB diagnosis; no definition for right ventricular hypertrophy/failure given	Right ventricular hypertrophy/failure in 5.4%	G: 1, 2, 4, 5, 8, 9 P: 3, 6, 7, 10 N: 4, 8, 11 Main concerns: methodology relating to determination of RVH/failure unclear; reported as an additional outcome; analysis not described

Reviewed studies regarding management outcomes relating to non-acute management of chronic obstructive pulmonary disease (COPD). All were cross-sectional studies. Population characteristics are entered as available. Studies of quality concern (see Methods) are entered in italics, with the main concerns being noted in the 'Quality' column. The numbers following the different quality 'levels' (G, P, N) indicate the aspect of quality assessment (see Box 1), rated as good (G), poor (P) or not-assessable (N)

GOLD, Global Initiative for Chronic Obstructive Lung Disease; PHQ-9, Patient Health Questionnaire-9; PEFR, peak expiratory flow rate; CB, chronic bronchitis

associated with more recent studies. Many outcomes were considered: prevalence of depression, cor pulmonale, osteopaenia and osteoporosis, disability and distress scores, mortality data and management of smoking. The only process measures investigated were some relating to management of smoking.

COPD was associated with relatively high levels of depression, disability and distress.<sup>43,46</sup> It was the second commonest cause of death generally, and the highest in older age groups.<sup>45</sup> The observed extent of right ventricular failure/cor pulmonale was low – but both of the investigating studies were relatively dated.<sup>48,49</sup> The prevalences of osteoporosis and osteopaenia were insufficiently different from estimates of general populations of the same age to be able to convincingly suggest a difference in the absence of a control group.<sup>44</sup> The study relating to education and treatment of smoking had some quality concerns, but suggested that only 88.7% of patients received cessation advice, and one-third of patients were unaware of the association between COPD and smoking.<sup>47</sup> Excluding studies with quality concerns, only those investigating depression, disability and distress remained.

## Discussion

### Principal findings

We planned an investigation to determine the extent and efficacy of the management of COPD in India. An important observation was the paucity of data and inconsistency in study setting and population characteristics. This is in contrast to some other states, such as in England, where national studies have demonstrated the availability/efficacy of current management across the region.<sup>50</sup> Study quality was also variable and of concern in 19/36 cases, but improved in recent years. These issues so impacted on analysis that we were unable to draw conclusions regarding efficacy of management under current strategies, and the extent of applicability of trialled interventions.

Data regarding management outcomes were particularly lacking. Of the few available studies, many were not conceived with this in mind, the studies were few and disparate and only two were deemed of reliable quality. They were

certainly suggestive that outcomes are suboptimal, but being carried out on various ill-defined management backgrounds and varied populations, over an extended time-period, their degree of general applicability is relatively unknown.

Uncertainty is again an issue in interpretation of the review of management interventions – almost all of which showed success in at least some outcome measures. This is especially so when, for example, pulmonary rehabilitation (a component of current guidelines) remains a subject of investigation and generates a positive response. Such data – and the one study of process measures suggestive that smoking cessation advice (another component of the guidelines) is not consistently delivered<sup>44</sup> – emphasize the need for the extent of current guideline implementation to be understood, before studies such as those reviewed can be most usefully applied.

The issue of the optimal extent of generalization of trialled interventions is in many respects premature. However, subgroup differences in disease prevalence, nature and course will exist, differential management strategies may be useful, and this can be usefully borne in mind as investigations continue.

### Strengths and weaknesses of this study

Although the low number and heterogeneity of the reviewed studies were a notable outcome in themselves, they did have a considerable effect on the extent to which this review could be undertaken as planned. Further limitations on our results were imposed by (1) aspects of the review methodology and (2) our decision not to include unpublished data from trial databases.

The methodology was constrained in particular by the subjective nature of the quality assessment, and the lack of appropriateness of data for meta-analysis. The data were insufficient even for narrative synthesis in some areas of investigation. Regarding our decision not to include data from trial databases, we accept that our thus relatively constrained inclusion criteria may have increased the possibility of reporting bias. Indeed the observed outcomes regarding management interventions would allow that these data may have been at risk of publication bias.

We hope, though, that our thorough, systematic approach has identified most of the available data, and helped to provide a useful, clear summary, demonstrative of where the gaps in knowledge lie.

### Interpretation of findings in relation to previously published work

Comparing outcomes of COPD management in India with those elsewhere is hindered mainly by the paucity of data. The management guidelines utilized in India are based on those recommended by international bodies and utilized elsewhere. They reflect disease pattern and context in India to an extent,<sup>51</sup> but do not really reflect that the included strategies tend to have been developed from study of populations resident in more developed states, and that the extent to which they can be similarly applied to other populations – including Indian populations – is unclear. The reviewed intervention and outcome studies are indicative that aspects of the current programme should be beneficial, but further study is required to determine that the guidelines are sufficiently effective in this population, and to investigate any subpopulation subtleties with regard to treatment outcomes. For example, the nature of the disease associated with domestic, and other environmental, pollution (relatively prevalent in this population) – rather than that associated with smoking – is less well characterized. Similarly, the nature of the disease when associated with HIV/tuberculosis is unclear,<sup>3</sup> and issues such as poor nutrition may well be of relevance to management.<sup>6</sup>

Study of primary prevention was conspicuously lacking. The existing management guidelines do include reduction of risk factors, but these need to be implemented as more general societal measures (i.e. as primary rather than secondary prevention), and it is not clear that this is being achieved. Although a smoking ban was introduced in India in 2008, media reports of successful implementation of the ban are mixed. Ensuring achievement of the ban is a priority, and additional programmes such as those modelled by Wilkinson *et al.*<sup>14</sup> and further demotion of smoking activities, would be of use. The reviewed study of a smoking cessation

programme<sup>15</sup> was difficult to interpret, but it is likely cessation programmes would be usefully applied – particularly when associated with an education component – for which there is an evident need.<sup>47,52</sup> A review of smoking cessation programmes in India, their outcomes and associated research, would probably be useful.

### Implications for future research, policy and practice

Although many of the studies reviewed here do contain potentially useful management strategies, these options, and others, could be better assessed and implemented if the distribution and success of current management was better understood. It might be useful to initially:

- (1) Achieve a better understanding of disease prevalence and likely trends in prevalence, as we have recently suggested;<sup>9</sup>
- (2) Audit the use of guidelines – in terms of both process and clinical outcomes – across the country;
- (3) Estimate the proportion of the population accessing health-care services, and the proportion to which optimal/guideline care is available and taken-up.

This information would provide a useful background on which study of more subtle themes – such as those relating to the nature of disease among subgroups, and how best to target resources – could be based.

In the interim, the lack of data should not preclude the implementation of potentially useful interventions. Our review has shown that many secondary prevention methods would be beneficial, and that primary prevention methods are especially needed, and could be usefully implemented with ongoing review. In addition to consideration of change in domestic fuel use and tackling the extent of smoking, occupational health is another important primary prevention issue. In our review, we excluded studies investigating occupational groups alone, but several occupational groups are understood to be at relatively great risk,<sup>53</sup> and need particular attention, especially in terms of preventive interventions.



## Conclusions

Investigation of the current extent of management of COPD in India is hindered by the number and nature of studies available. High-quality current data from a cross-section of the population is required if the current quality of management is to be determined at a level useful for policy considerations. An understanding of the extent of implementation of national guidelines would be particularly useful, and it would also be helpful to understand the current use of important preventive measures, particularly those targeting smoking, domestic fuel use and occupational risk. This would provide a useful background on which the efficacy of further management strategies – including some of those successfully trialled to date – could be usefully examined. The specific needs of subgroups could also then be further investigated and addressed.

In addition, optimal long-term solutions will require provision of more comprehensive prevalence estimates than are currently available, review of the changing context of service delivery and implementation of a more general approach to chronic disease management.

## References

- 1 Global Risks 2010: A Global Risk Network Report, World Economic Forum, January 2010, World Economic Forum, 2010
- 2 Report of the Secretary General. *Prevention and Control of Non-communicable Diseases*. Item 119; United Nations 66th session, 2011. See [http://www.un.org/ga/search/view\\_doc.asp?symbol=A/66/83&Lang=E](http://www.un.org/ga/search/view_doc.asp?symbol=A/66/83&Lang=E) (last accessed December 2011)
- 3 Chan-Yeung M, Ait-Khaled N, White N, Ip MS, Tan WC. The burden and impact of COPD in Asia and Africa. *Int J Tuberc Lung Dis* 2004;8:2–14
- 4 World Health Organisation. Chronic obstructive pulmonary disease (COPD) Fact sheet No 315. World Health Organization, 2011. See <http://www.who.int/mediacentre/factsheets/fs315/en/index.html> (last accessed July 2011)
- 5 Department of Measurement and Health Information Systems of the Information, Evidence and Research Cluster. World Health Statistics 2008. World Health Organization, 2008. See [http://www.who.int/whosis/whostat/EN\\_WHS08\\_Full.pdf](http://www.who.int/whosis/whostat/EN_WHS08_Full.pdf) (last accessed August 2011)
- 6 Caszo B, George A, Souza D. COPD and nutrition. *Lung India* 2006;23:78–81
- 7 World Health Organisation, Department of Health Statistics and Informatics; Information, Evidence and Research Cluster. The Global Burden of Disease 2004 Update. World Health Organization, 2008
- 8 Celli BR, Cote CG, Marin JM, *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. See <http://dx.doi.org/10.1056/NEJMoa021322> (last accessed 27 September 2012)
- 9 McKay AJ, Mahesh PA, Fordham JZ, Majeed A. Prevalence of COPD in India: a systematic review. *Prim Care Resp J* 2012;21. See URL: <http://dx.doi.org/10.4104/pcrj.2012.00055>
- 10 Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097. See <http://dx.doi.org/10.1371/journal.pmed.1000097>
- 11 Centre for Reviews and Dissemination. *Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care*. Centre for Reviews and Dissemination, University of York, 2008. See [http://www.york.ac.uk/inst/crd/pdf/Systematic\\_Reviews.pdf](http://www.york.ac.uk/inst/crd/pdf/Systematic_Reviews.pdf) (last accessed April 2011)
- 12 Effective Public Health Practice Project. Quality Assessment Tool for Quantitative Studies. See <http://www.ephpp.ca/Tools.html>. (last accessed 5 August 2012)
- 13 The Cochrane Collaboration. *Cochrane Handbook for Systematic Reviews of Interventions*. See <http://www.cochrane-handbook.org/>. (last accessed 5 August 2012)
- 14 Wilkinson P, Smith KR, Davies M, *et al*. Public health benefits of strategies to reduce greenhouse-gas emissions: household energy. *Lancet* 2009;374:1917–29. See [http://dx.doi.org/10.1016/S0140-6736\(09\)61713-X](http://dx.doi.org/10.1016/S0140-6736(09)61713-X) (last accessed 27 September 2012)
- 15 Vaishal PS, Narayana RS, Pramo PS. Nicotine de-addiction facility needs in rural Indian community: NGO initiatives in phase-iv community project. Conference Publication: 11th World Congress of Psycho-Oncology of the International Psycho-Oncology Society, Vienna, Austria, 2009. *Psycho-Oncol* 2009;18:S226–7
- 16 Rao RS, Singh S, Sharma BB, Agarwal VV, Singh V. Sildenafil improves six-minute walk distance in chronic obstructive pulmonary disease: a randomised, double-blind, placebo-controlled trial. *Indian J Chest Dis Allied Sci* 2011;53:81–5
- 17 Sindhwani G, Verma A, Biswas D, Srivastava M, Rawat J. A pilot study on domiciliary pulmonary rehabilitation program in the management of severe COPD. *Singapore Med J* 2011;52:689–93
- 18 Dalvi PS, Singh A, Trivedi HR, Ghanchi FD, Parmar DM, Mistry SD. Effect of doxycycline in patients of moderate to severe chronic obstructive pulmonary disease with stable symptoms. *Ann Thorac Med* 2011;6:221–6
- 19 Subin RV, Prem VS. Effect of upper limb, lower limb and combined training on health-related quality of life in COPD. *Lung India* 2010;27:4–7
- 20 Mohan V, Henry LJ, Roslizawati N, Das S, Kurup M, Gopinath B. Effect of unsupported arm exercises on spirometry values and functional exercise tolerance of subjects with chronic obstructive pulmonary disease. *Int Med J* 2010;17:113–6
- 21 Brashier B, Dhembare P, Jantikar A, *et al*. Tiotropium administered by a pressurized metered dose inhaler (pMDI) and spacer produces a similar bronchodilator response as that administered by a Rotahaler® in adult subjects with stable moderate-to-severe COPD. *Resp Med* 2007;101:2464–71. See <http://dx.doi.org/10.1016/j.rmed.2007.07.006> (last accessed 27 September 2012)



- 22 Janmeja AK, Mohapatra PR, Kumar M. The impact of 'World Health Organization – Government of India guidelines on chronic obstructive pulmonary diseases-2003' on quality of life. *Lung India* 2009;**26**:102–5
- 23 Chhabra SK, Vijayan VK, Vasu T. Inhaled formoterol versus ipratropium bromide in chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci* 2006;**48**:97–102
- 24 Murali PM, Rajasekaran S, Paramesh P, et al. Plant-based formulation in the management of chronic obstructive pulmonary disease: a randomized double-blind study. *Resp Med* 2006;**100**:39–45. <http://dx.doi.org/10.1016/j.rmed.2005.04.011> (last accessed 27 September 2012)
- 25 Chhabra SK, Ailawadhi M. Effect of prednisolone on lung function and bronchodilator responses in stable COPD. *Lung India* 2006;**23**:8–14. See <http://dx.doi.org/10.4103/0970-2113.44424> (last accessed 27 September 2012)
- 26 Katiyar SK, Bihari S. Role of pranayama in rehabilitation of COPD patients – a randomised controlled study. *Indian J Allergy Asthma Immunol* 2006;**20**:98–104
- 27 Prakash O, Kumar R, Rahman M, Gaur SN. The clinic-physiological effect of inhaled tiotropium bromide and inhaled ipratropium bromide in severe chronic obstructive pulmonary disease. *Indian J Allergy Asthma Immunol* 2006;**20**:105–11
- 28 Zaidi SAR, Ahmad MA, Aslam KM, Rauf A, Mukherjee AK. Clinical study to evaluate the efficacy of a compound unani herbal formulation sharbat-e-unsul murakkab in sual-el-muzmin (chronic bronchitis). *Aust J Med Herbalism* 2010;**22**:89–93
- 29 Menon B, Gurnani M, Aggarwal B. Comparison of outpatient visits and hospitalisations, in patients with chronic obstructive pulmonary disease, before and after influenza vaccination. *Int J Clin Pract* 2008;**62**:593–8. See <http://dx.doi.org/10.1111/j.1742-1241.2007.01641.x> (last accessed 27 September 2012)
- 30 Pande A, Singhal P, Kumar R, Gaur SN. Effect of home-based pulmonary rehabilitation programme on disability in patients with chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci* 2005;**47**:217–9
- 31 Bachh AA, Shah NN, Bhargava R, et al. Effect of oral N-acetylcysteine in COPD – a randomised controlled trial. *JK Pract* 2007;**14**:12–6
- 32 Nadeem A, Raj HG, Chhabra SK. Effect of vitamin E supplementation with standard treatment on oxidant-antioxidant status in chronic obstructive pulmonary disease. *Indian J Med Res* 2008;**128**:705–11
- 33 Daga MK, Chhabra R, Sharma B, Mishra TK. Effects of exogenous vitamin E supplementation on the levels of oxidants and antioxidants in chronic obstructive pulmonary disease. *J Biosci* 2003;**28**:7–11
- 34 Singh V, Khandelwal DC, Khandelwal R, Abusaria S. Pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci* 2003;**45**:13–7
- 35 Guleria R, Singh TR, Sinha S, Padhy K, Gupta K, Pande JN. Effect of single inhalation of a salbutamol, ipratropium bromide and beclomethasone on mucociliary clearance in patients with chronic obstructive airway disease. *Indian J Chest Dis Allied Sci* 2003;**45**:241–46
- 36 Gupta RK, Chhabra SK. An evaluation of salmeterol in the treatment of chronic obstructive pulmonary diseases. *Indian J Chest Dis Allied Sci* 2002;**44**:165–72
- 37 Mahesh PA, Parthasarathi G, Jayaraj BS, Thomas A, Palaksha S. Assessment and comparison of quality of life in COPD patients receiving ipratropium and sustained release theophylline. *Lung India* 2001;**19**:9–15
- 38 Bhargava R, Sharma DK, Chauhan JS. Combination therapy with salbutamol and ipratropium bromide in stable patients of chronic obstructive pulmonary disease. *Lung India* 1999;**17**:15–8
- 39 Behera D. Yoga therapy in chronic bronchitis. *J Assoc Physicians India* 1998;**46**:207–8
- 40 Ray D, Rajaratnam A. Relative functional efficacy of methylxanthine and beta2 agonists in maintenance therapy of COPD. *Lung India* 1991;**9**:82–5
- 41 Premanand R, Reddy CS, Sundaramma M. Ipratropium bromide and salbutamol inhalations in asthma and chronic bronchitis. *Lung India* 1989;**2**:26–30
- 42 Kulpati DDS, Kamath RK. The influence of physical conditioning by yogasanas and breathing exercises in patients of chronic obstructive pulmonary disease. *Lung India* 1982;**1**:35–8
- 43 De S. Prevalence of depression in stable chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci* 2011;**53**:35–9
- 44 Bhattacharyya P, Paul R, Ghosh M, et al. Prevalence of osteoporosis and osteopenia in advanced chronic obstructive pulmonary disease patients. *Lung India* 2011;**28**:184–6. See <http://dx.doi.org/10.4103/0970-2113.83974> (last accessed 27 September 2012)
- 45 Saha R, Nath A, Sharma N, Badhan SK, Ingle GK. Changing profile of disease contributing to mortality in a resettlement colony of Delhi. *Nat Med J India* 2007;**20**:125–7
- 46 Joshi K, Kumar R, Avasthi A. Morbidity profile and its relationship with disability and psychological distress among elderly people in Northern India. *Int J Epidemiol* 2003;**32**:978–87. See <http://dx.doi.org/10.1093/ije/dyg204> (last accessed 27 September 2012)
- 47 Behera D. Attitude of chronic bronchitic patients towards smoking. *Lung India* 1992;**10**:138–9
- 48 Ray D, Abel R, Selvaraj KG. A 5-yr prospective epidemiological study of chronic obstructive pulmonary disease in rural south India. *Indian J Med Res* 1995;**101**:238–44
- 49 Nigam P, Verma BL, Srivastava RN. Chronic bronchitis in an Indian rural community. *J Assoc Physicians India* 1982;**30**:277–80
- 50 Calderon-Larranaga A, Carney L, Soljak M, et al. Association of population and primary healthcare factors with hospital admission rates for chronic obstructive pulmonary disease in England: national cross-sectional study. *Thorax* 2011;**66**:191–6. See <http://dx.doi.org/10.1136/thx.2010.147058> (last accessed 27 September 2012)
- 51 WHO-Government of India Biennium (2002–2003) Programme. Guidelines for Management of Chronic Obstructive Pulmonary Disease (COPD) in India: a guide for physicians (2003). *Indian J Chest Dis Allied Sci* 2004;**46**:137–53
- 52 Mahesh PA, Jayaraj BS, Prahlad ST, et al. Validation of a structured questionnaire for COPD and prevalence of COPD in rural area of Mysore: a pilot study. *Lung India* 2009;**26**:63–9. See <http://dx.doi.org/10.4103/0970-2113.53226> (last accessed 27 September 2012)
- 53 Boschetto P, Quintavalle S, Miotto D, Lo Cascio N, Zeni E, Mapp CE. Chronic obstructive pulmonary disease (COPD) and occupational exposures. *J Occup Med Toxicol* 2006;**1**:11–6

## Appendix

### QUOROM Statement checklist

Review of chronic obstructive pulmonary disease management outcomes in India				
Heading	Subheading	Descriptor	Reported? (Y/N)	Page number
Title		Identify the report as a systematic review	Y	1
Abstract		Use a structured format	Y	1
	Objectives	The clinical question explicitly	Y	1
	Data sources	The databases (i.e. list) and other information sources	Y	1
	Review methods	The selection criteria (i.e. population, intervention, outcome and study design); methods for validity assessment; data abstraction; and study characteristics and quantitative data synthesis in sufficient detail to permit replication	N	1
	Results	Characteristics of the randomized controlled trial included and excluded; qualitative and quantitative findings (i.e. point estimates and confidence intervals) and subgroup analyses	Y	1
	Conclusion	The main results <b>Describe</b>	Y	1
Introduction		The explicit clinical problem, biological rationale for the intervention and rationale for review	Y	2
Methods	Searching	The information sources, in detail (e.g. databases, registers, personal files, expert informants, agencies and hand-searching) and any restrictions (years considered, publication status and language of publication)	Y	2, 3
	Selection	The inclusion and exclusion criteria (defining population, intervention, principal outcomes and study design)	Y	3, Tables 1 and 2
	Validity assessment	The criteria and process used (e.g. masked conditions, quality assessment and their findings)	Y	5, 6
	Data abstraction	The process or processes used (e.g. completed independently, in duplicate)	Y	5, 6
	Study characteristics	The type of study design, participants' characteristics, details of intervention, outcome definitions and how clinical heterogeneity was assessed	Y	5, 6, Tables 3–5
	Quantitative data synthesis	The principal measures of effect (e.g. relative risk), method of combining results (statistical testing and confidence intervals), handling of missing data; how statistical heterogeneity was assessed; a rationale for any <i>a priori</i> sensitivity and subgroup analyses and any assessment of publication bias	N/a	No quantitative synthesis performed
Results	Trial flow	Provide a meta-analysis profile summarizing trial flow (see Figure 1)	N/a	N/A

(Continued)

Continued				
Heading	Subheading	Descriptor	Reported? (Y/N)	Page number
	Study characteristics	Present descriptive data for each trial (e.g. age, sample size, intervention, dose, duration and follow-up period)	Y	6, 18, Tables 3–5
	Quantative data synthesis	Report agreement on the selection and validity assessment; present simple summary results (for each treatment group in each trial, for each primary outcome); present data needed to calculate effect sizes and confidence intervals in intention-to-treat analyses (e.g. 2 × 2 tables of counts, means and standard deviations, proportions)	Y	6, 18, quantitative data synthesis does not apply
Discussion		Summarize key findings; discuss clinical inferences based on internal and external validity; interpret the results in light of the totality of available evidence; describe potential biases in the review process (e.g. publication bias) and suggest a future research agenda	Y	18–20

© 2012 Royal Society of Medicine Press

This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by-nc/2.0/>), which permits non-commercial use, distribution and reproduction in any medium, provided the original work is properly cited.