Version 3, March 2011

Arthritis Research UK Primary Care Centre
Systematic Review Protocol & Support Template

This template is primarily intended to help you plan your review in a systematic way. A copy of this completed form will be available via the intranet to help others carrying out reviews in the future and to avoid duplicating work already undertaken in the Centre. Keeping a record of all the reviews will also assist in planning the work of the Centre and ensuring adequate methodological support. Not all the information will be relevant to every review. However, items can be adapted to fit the type of review that is being undertaken.
Please complete the form in as much detail as possible for your review and email to Jo Jordan, j.jordan@cphc.keele.ac.uk

Title of the review	*A systematic review to examine the relationship of anxiety and depression to exacerbations of COPD, that result in hospital admissions, and if there are other mediating factors involved*
First reviewer	*Dr Alison Pooler*
Team of reviewers	*Dr Roger Beech* *Dr Fay Foster*
Supervisor/Project PI	*Dr Roger Beech* *Prof Sue Read*
Clinical Portfolio Group	*Dr Martin Allen, consultant physician, Respiratory Medicine, UHNS* *Dr Rosie Piggott, GP, Milton,Dr Fay Foster, Researcher and Psychologist*
Project title (if different from review title)	

Support – please state if advice/training or personnel required at each stage	
SR overview	*Advice sought from Jo Jordon, Krysia, and Roger*
Protocol development	“”
Literature searching	*Already had training from library on literature searching and RefWorks and also did literature review for PhD study*
Quality appraisal	*Advice gained from Jo Jordon and from reading around the area*
Data Extraction	“”
Synthesis	“”

Writing up	“”

1. Background to review

Brief introduction to the subject of the review, including rationale for undertaking the review and overall aim

COPD is a major cause of chronic morbidity and mortality worldwide. The 2002 World Health Report (WHO, 2002), listed COPD as the fifth leading cause of death in the world, and further increases in its prevalence and mortality are expected to make it the third leading cause of mortality by 2015 (Murrey & Lopez, 1997). COPD is a complex disease, triggered mostly by exposure to cigarette smoking, and leads not only to pulmonary damage, but also to systematic impairment. There is also growing awareness of systematic inflammation, cardiovascular, neurologic, psychiatric and endocrine morbidities that are common co morbidities of the condition and having a detrimental effect on the long term morbidity and mortality of COPD (Jennings et al, 2009).

COPD has a major effect on health status, particularly in terms of impaired exercise performance and functional capacity. The presence of daily symptoms and a high exacerbation frequency are other important factors (Ozkaya et al, 2011). COPD also accounts for many visits to health care professionals in the UK. General practitioner consultations for COPD in one year, range from 4.17 per 1000 in people aged 45-64 years, to 8.86 per 1000 in 65-74 years, to 10.32 per 1000 in 75-84 year olds (Calverley, 1998; Pauwels et al, 2004). These rates are four times those for chest pain caused by ischaemic heart disease. Exacerbations are also an important cause of hospitalisation and are responsible for about 10% of all acute medical admissions (Miravitlles et al, 2002)

Exacerbations of COPD are a major cause of increased morbidity, hospital admissions and mortality, and strongly influence the health related quality of life for the sufferer (Wedzicha et al, 2003). Donaldson et al (2002), demonstrated that the frequency of occurrence of acute exacerbations contributed to long term decline in lung function in COPD. They showed that patents with COPD who suffered frequent exacerbations, experienced a significantly greater decline in FEV1, than patients who had infrequent exacerbations. Exacerbations are more common than previously believed (2.5-3 per year(mean)) (Wedzicha et al, 2003). Also, following an exacerbation, the incomplete recovery of lung function after the event, means that the patient may not regain his or her stable lung function, which may contribute to a decline in lung function with time, which is characteristic of COPD (Seemungal et al, 2000; Donaldson et al, 2002). These findings emphasise the importance of targeting COPD exacerbations to reduce disease progression and particularly, to detect patients who are frequent exacerbators, and the underlying factors that drive these exacerbations. COPD is a largely preventable and treatable disease that is responsible for a substantial human and economic burden and there is a need to target specific factors that contribute to such suffering.

Anxiety and depression are common co morbidities of COPD (Andenaes et al, 2004; Yohannes et al, 2005; Gudmundsson et al, 2006). There is literature that illustrates the presence of these co morbidities and also suggests that there may be some relationship between these co morbidities and exacerbations of COPD (Fan et al, 2002). This literature is not however conclusive (Garcia-Aymerich et al, 2003; Peruzza et al, 2003), due to different tools being used to measure anxiety and depression and also studies being done in different countries which have non-comparable health services and some studies that included asthmatics as well as people with COPD. Untreated or incompletely treated depression and anxiety may also have major implications for compliance with medical treatment, due to the effects on cognitive functioning and the decreased effectiveness of any self-management activities that the person may instigate (Bosley et al, 1996; Kunik et al, 2005; Gudmundsson et al, 2006). The way in which anxiety and depression may be associated with COPD exacerbations may also have a relationship with this issue of ineffective coping and self- management strategies adopted by the patients. Depression may also be a significant predictor of mortality following hospitalisation for acute exacerbation (Almagro et al, 2002).

The research to be undertaken as a component of the fellowship will help to build on this as yet inconclusive evidence to elucidate the relationship between these co morbidities and exacerbations of COPD, but more importantly, explore the link between exacerbations and the characteristics of current approaches to management and self-management amongst people who also have anxiety and depression. Findings will inform the development of strategies for reducing exacerbations and hospitalisations in this patient group that could be tested in a subsequent research proposal.

Aim

To examine the relationship of anxiety and depression to exacerbations of COPD that result in hospital admission, and to investigate whether there are other mediating factors involved. The understanding may allow potentially effective interventions for improving management and self-management to be designed and later systematically evaluated in more in-depth studies

2. Specific objectives

1. *To clarify the evidence base available around the relationships of anxiety and depression to exacerbations of COPD, that lead to hospital admissions. Clarification will be made by a systematic review of the evidence base of journals and abstracts in this topic area, looking at all designs of study.*

2. *To identify any other factors in these patients that are thought to also be involved in their admission. Along with the co-morbidities of anxiety and depression. These other factors include ability to cope and self-manage their condition and also other co morbidities and social factors that may affect their ability to cope or self-manage. This cannot be more specific until an examination of the evidence is done*

3. a) Criteria for including studies in the review If the PICOS format does not fit the research question of interest, please split up the question into separate concepts and put one under each heading	
i. Population, or participants and conditions of interest	*People with COPD; any age, any gender and any severity of COPD* *Population not restricted to the UK, will examine papers from all over the world*
ii. Interventions or exposures	*People who have been admitted to hospital with an exacerbation of COPD, who have the co-mobidites of anxiety and depression*
iii. Comparisons or control groups	*People who have been admitted to hospital with an exacerbation of COPD with no psychological co morbidities*
iv. Outcomes of interest	*Prevalence/presence of psychological co-morbidities and numbers of hospital admission for exacerbation of COPD*
v. Setting	*Hospital admissions/secondary care*
vi. Study designs	*Any study design: would expect to be observational/cohort studies rather than RCT's*

3. b) Criteria for excluding studies not covered in inclusion criteria Any specific populations excluded, date range, language, whether abstracts or full text available, etc

If patient have asthma or any other respiratory disease *Studies that don't relate the presence of the co morbidities of anxiety and depression to exacerbation of COPD*

4. Search methods	
Electronic databases Please list all databases that are to be searched and include the interface (eg NHS, EBSCO, etc) and date ranges searched for each	*PUBMED/MEDLINE* *COCHRANE* *EMBASE* *Cinhal* *PsychInfo* *Keele Web of Science* *CDR/DARE databases*
Other methods used for identifying relevant research ie contacting experts and reference checking	*Reference checking and hand searching of these.* *Contacting experts in this field/DOH/BTS/NICE* *Identifying possible data from conferences attended*
Journals hand searched If any are to be hand searched, please list which journals and date searched from, including a rationale.	*Journal of psychosomatic medicine* *Social science and medicine* *I have decided to hand search these journals as I found many articles about psychological factors in asthma in them while doing my PhD but this journal has not shown up in the electronic data base search.*

5. Methods of review	
Details of methods Number of reviewers, how agreements to be reached and disagreements dealt with, etc.	*Two main reviewers and a third to resolve any disagreements* *Main reviewers myself, Fay and third reviewer Roger* *Agree data to be extracted and terminology used in CPD to be clarified before hand*
Quality assessment Tools or checklists used with references or URLs	*Protocol will define the method of literature critique/ appraisal use, and will use STROBE tool for relevant content and methodology used in the each of the papers to be reviewed*
Data extraction What information is to be collected on each included study. If databases or forms on Word or Excel are used and how this is recorded and by how many reviewers	*Data extraction form in Word document* *RefWorks to be used to keep track of references* *Reviewer number 1 (ap) will review first, followed by reviewer number 2 (ff), which will be done independently. If necessary reviewer number 3 will review if there are any disparities between the two initial reviews*
Narrative synthesis Details of what and how synthesis will be done	*Narrative synthesis will be done alongside any meta-analysis and will be carried out using a framework which consists of four elements;* 1. *Developing a theory of how the intervention works, why and for whom* 2. *Developing a preliminary synthesis of findings of included studies* 3. *Exploring relationships within and between studies* 4. *Assessing the robustness of the synthesis*
Meta-analysis Details of what and how analysis and testing will be done. If no meta-analysis is to be conducted, please give reason.	*Although a meta-analysis is planned this will only become apparent when we see what data is extracted and made available from the systematic review.* *Need to think about how heterogenitiy will be explored*

Grading evidence System used, if any, such as GRADE	N/A

6. Presentation of results	
Additional material Summary tables, flowcharts, etc, to be included in the final paper	*Flow chart of whole process* *Protocol* *Data extraction form and tables* *Forest plots of studies included in the final review*
Outputs from review Papers and target journals, conference presentations, reports, etc	*X1 paper in high quality respiratory journal (Thorax has the highest impact factor, followed by Respiratory Medicine)* *Conference presentations at BTS* *Report to the DOH steering group for respiratory research and the strategy group for outcomes of COPD and asthma UK* *Report/presentation to UHNS/Pct. boards* *Report and presentation to fellowship board in 12 months*

7. Timeline for review – when do you aim to complete each stage of the review	
Protocol	*1 month*
Literature searching	*2 months*
Quality appraisal	*2 months*
Data extraction	*2 months*
Synthesis	*2 months*
Writing up	*2 months*

Please send your completed protocol to Jo Jordan (see email below) as we would like to put these on the Intranet.

The systematic review team are available to answer any queries or give advice on completing your review. Systematic review workshops are run at least once a year, or can be arranged on an ad hoc basis if needed by a group. Presentations from previous workshops can be found on the Centre's Intranet.

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