CareSearch Project Research Studies Register: Registration Proforma	0084

Study Title: Opioids in Dyspnoea an open label, prospective, dose ranging effectiveness study of sustained-release opioids in the subjective sensation of dyspnoea in opioid naive patients in the palliative care setting.

Brief description of the study:

Background: Breathlessness is a very distressing and difficult symptom commonly experienced towards the end of life. There are published research findings to show that the use of low dose long acting morphine can help the sensation of breathlessness, without side effects such as drowsiness and respiratory depression. There are now even lower doses of sustained release morphine available than when initial studies were done which may offer similar benefits and potentially fewer side effects. Initial studies in this area were short (one week) and long term benefits and side effects have not been well studied.

Study Design: This will be done through the use of a 2 stage open label study. In Stage 1, consenting participants will start on a small dose (10 mg) of slow release morphine for one week and if there is benefit, proceed to Stage 2. If there is no benefit, the dose will be increased to 20mg each morning, and the evaluation repeated. The maximum dose will be 30mg, and if there has been no benefit at this dose, the person will not proceed with the study. Participants will be asked to complete a simple twice daily diary throughout Stage 1, and will be monitored by visits to their home weekly and telephone calls between visits by the study nurse. In Stage 2 participants will be asked to continue on the morphine dose, determined in Stage 1, long term to determine if that dose continues to provide benefit. They will then be monitored by regular telephone calls for the duration of the study and will also be asked to maintain a simple weekly diary for this time to provide ongoing information about their response to the morphine and any side effects.

Objectives: The aims of Stage 1(open label dose ranging) are to determine the lowest effective dose of sustained release (SR) morphine for the relief of dyspnoea and the frequency and range of dose limiting side effects and for Stage 2 (long term effectiveness study) to determine if the dose of SR morphine remains effective in the control of dyspnoea over time and if other side effects emerge.

Outcomes and measures : The primary outcome is the sensation of dyspnoea as an average of both the morning and evening scores of the previous 3 days (before the census points) measured by the VAS (Visual Analogue Scale) for breathlessness which participants will record twice daily in their Stage 1 diary. The secondary outcomes are to document and compare differential side effects and participant burden from varying doses and to document and determine the long term benefit of the dose, measured by the McGill Quality of Life Questionnaire, the Modified Medical Research Council (MRC) dyspnoea scale, the Dyspnoea Exertion Scale (DES), descriptors of dyspnoea and side effects measured by descriptor scales and Visual Analogue Scales.

Analysis: Sample size is based on data from at least 25 patient years of data from the start of Stage 2 (for example, a participant who contributed 3 months of data would be equivalent to 0.25 years of data.) It is estimated that we will need to recruit approximately 100 participants to accrue this number.

Study Methodology: (Please mark with an x which type of study methodology)

	Epidemiology
	Health Services / Health Economics / Quality Improvement
	Qualitative, Observational or Descriptive
	Mixed Method
	Systematic Review
	Intervention: RCT
X	Intervention: Comparative or cohort study

	Intervention: Case series						
Project details:							
Funding source (Optional): **NHMRC project grant No. 380459**							
Has the study received ethics approval?	**X**	Yes		No		Not applicable	
Project starting date: **April 2006**							
Project completion date**:** **December 2009**							
Multi site:	**X**	Yes		No		Not applicable	

RESEARCHERS

Principal Investigator (name)	**Prof. David Currow**
Contact Details	**Department of Palliative and Supportive Services , Flinders University** **700 Goodwood Road, DAW PARK SA 5041** **Ph: (08) 8275 1732 , Fax: (08) 8374 0350 , Mobile: 0401 710 240** **E-mail: david.currow@health.sa.gov.au**
Investigator B (Name)	**Dr. Amy Abernethy**
Investigator C (Name)	**Dr. Michael Briffa**
Investigator D (Name)	**A/Prof Christine McDonald**
Investigator E (Name)	**Prof. Peter Frith**

Associated publications / reports:

Progress Report 2010.

Currow DC, Smith J, Davidson PM, Newton PJ, Agar MR, Abernethy AP. Do the trajectories of dyspnea differ in prevalence and intensity by diagnosis at the end of life? A consecutive cohort study. J Pain Symptom Manage. 2010 Apr;39(4):680-90.

Currow DC, Plummer JL, Crockett A, Abernethy AP. A community population survey of prevalence and severity of dyspnea in adults. J Pain Symptom Manage. 2009 Oct;38(4):533-45.

Rocker G, Horton R, Currow D, Goodridge D, Young J, Booth S. Palliation of dyspnoea in advanced COPD: revisiting a role for opioids. Thorax. 2009 Oct;64(10):910-5.

Topics:

- **Respiratory Symptoms and their treatment**
- **Drug Trial**