Institution: King's College London

Unit of Assessment: 1- Clinical Medicine

Title of case study: Early pulmonary rehabilitation reduces re-admissions and improves survival of patients admitted to hospital with acute flare-ups of chronic obstructive pulmonary disease (COPD)

1. Summary of the impact

King's College London (KCL) research has had substantial impact, through making strong contributions to international and national guidelines which recommend that pulmonary rehabilitation should be made available to all appropriate people with COPD, including those who have had a recent hospitalisation for an acute flare-up.

Recommendations citing our research include those published internationally by a Cochrane Review and the Global Initiative for Chronic Obstructive Lung Disease, and nationally in the UK by NICE and IMPRESS – which provides clinical leadership to the NHS. These recommendations have been taken up by the NHS and are also included in NHS Best Practice Guidance (2012). The Department of Health (2010) estimated "widespread use of pulmonary rehabilitation would bring substantial annual savings".

2. Underpinning research

The research of the KCL Clinical Respiratory Physiology Group led by Professor John Moxham (KCL, 1982 - present) has resulted in changes in the management of patients admitted to hospital with acute flare-ups or worsening ('exacerbations') of COPD. Hospitalisations for acute flare-ups of COPD are very common and are associated with significant numbers of deaths.

The research group studied muscle weakness and fatigue in COPD patients, as well as mechanisms for effective pulmonary rehabilitation. The group designed and ran two novel randomised controlled trials, reported in 2004 and 2010, comparing the results of early pulmonary rehabilitation, soon after flare-ups occurred, against results of the usual care (1,2). KCL research has had a very considerable impact in demonstrating that such exercise-based rehabilitation for patients admitted to hospital with acute exacerbation is both effective and cost-effective (1,2).

Downward spiral in patients with exacerbations of COPD: Patients with moderate to severe COPD are prone to exacerbations, often triggered by viral infections and frequently requiring admission to hospital. Exacerbations dramatically reduce patients' activity and, as a result, patients' muscles waste and they become weak. Following exacerbations, patients' activity levels remain low for prolonged periods. COPD patients who have had exacerbations are at greater risk of future exacerbations and admissions than stable COPD patients.

KCL's long-standing research into muscle weakness in COPD patients: The KCL research group has investigated the underlying causes of muscle weakness and fatigue in COPD patients (3). In the late 1990s KCL showed, along with others, that in COPD patients the strength of quadriceps muscles in the thighs was 30% less than in normal subjects (4). However, the strength of a muscle in the hand (the adductor pollicis) and of the diaphragm, a major muscle involved in breathing (when corrected for the hyperinflation of lungs commonly seen in COPD) were shown to be normal (5,6,7).

Further research into muscle fatigue in COPD patients: KCL developed tests, both volitional and non-volitional (using magnetic nerve stimulation), of the strength of muscles related to breathing, as well as other muscles, in patients with COPD (8). These showed that abdominal muscle strength was normal in COPD patients and that the diaphragm was extremely resistant to fatigue. Although the quadriceps muscles are weak in COPD patients, there is not widespread weakness of other muscles, except in patients with physical wasting (cachexia) (9).

The insights from this research indicated that patients with COPD get breathless when they exercise and therefore they exercise less. As a result their legs become weak. As the form, structure and biochemistry of their muscles change, exercise leads to early and excessive lactate production. Early lactate production causes breathlessness and reduces activity. The progressive decrease in activity makes the legs weaker and weaker.

Research supporting exercise-based rehabilitation: KCL work showed that exercise-based rehabilitation after COPD exacerbations could reverse this downward spiral. A randomised controlled study of pulmonary rehabilitation in the community, following hospitalisation for acute exacerbations of chronic obstructive pulmonary disease was reported in the *British Medical Journal* in 2004 (1). This demonstrated that early pulmonary rehabilitation is safe and effective, accelerates the reconditioning of patients' leg muscles, increases their strength and improves their metabolism, thereby decreasing the production of lactate when they exercise – which reduces breathlessness and increases their exercise capacity.

Research on re-exacerbation rates following exercise-based rehabilitation: Further research investigated rates of re-exacerbation following early pulmonary rehabilitation. The findings, reported in *Thorax* in 2010 (2) demonstrated – for the first time – that early pulmonary rehabilitation, significantly reduced re-admissions within three months from 33% to just 7%.

Quadriceps strength was approximately 20% higher in the early pulmonary rehabilitation group compared to the usual care group at three months. Exercise capacity was substantially better, the incremental shuttle walk distance improved by approximately 33% and the endurance shuttle walk by 90% (2). This has important implications for the NHS, as it is known that both the capacity for exercise and the strength of the quadriceps muscles are predictors of COPD patients' future use of healthcare services.

3. References to the research

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2. Seymour JM, Moore L, Jolley CJ, Ward K, Creasey J, Steier JS, Yung B, Man WD, Hart N, Polkey MI, **Moxham J**. Outpatient pulmonary rehabilitation following acute exacerbations of COPD. *Thorax* 2010:65:423–8.
3. Mills GH, Kyroussis D, Hamnegard CH, Polkey MI, Green M, **Moxham J**. Bilateral magnetic stimulation of the phrenic nerves from an anterolateral approach. *Am J Respir Crit Care Med.* 1996:154:1099–105.
4. Polkey MI, Kyroussis D, Hamnegard CH, Mills GH, Green M, **Moxham J**. Quadriceps strength and fatigue assessed by magnetic stimulation of the femoral nerve in man. *Muscle Nerve* 1996:19:549–55.
5. Polkey MI, Kyroussis D, Hamnegard CH, Mills GH, Green M, **Moxham J**. Diaphragm strength in Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med.* 1996:154:1310–7.
6. Polkey MI, Kyroussis D, Hamnegard CH, Mills GH, Hughes PD, Green M, **Moxham J**. Diaphragm performance during maximal voluntary ventilation in Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med.* 1997:155:642–8.
7. Harris ML, Luo YM, Watson AC, Rafferty GF, Polkey MI, Green M, **Moxham J**. Adductor pollicis twitch tension assessed by magnetic stimulation of the ulna nerve. *Am J Respir Crit Care Med.* 2000:162:240–5.
8. Man WD, Soliman MG, Nikoletou D, Harris ML, Rafferty GF, Mustafa N, Polkey MI, **Moxham J**. Non-volitional assessment of skeletal muscle strength in patients with chronic obstructive pulmonary disease. *Thorax* 2003:58:665–9.
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4. Details of the impact

Chronic obstructive pulmonary disease (COPD) is a major public health problem. In 2020, COPD is projected to rank fifth worldwide in burden of disease. Three million people in England have COPD and currently there are 100,000 admissions for exacerbation of COPD in England each year. Mortality is high in patients admitted to hospital (1 in 12 die during admission and 1 in 6 die within three months of an admission). By avoiding re-admissions, early pulmonary rehabilitation – a combination of interventions on the respiratory system (i.e. stopping smoking, optimisation of medication), psychological support (i.e. patient education, psychological and social support) and, importantly, physical exercise – stabilises or reverses COPD and avoids premature deaths.

Strong contribution to evidence base for pulmonary rehabilitation in patients with unstable COPD: A very significant impact resulting from KCL research is a strong contribution to the Cochrane Review of pulmonary rehabilitation in patients with unstable COPD (10). Cochrane Reviews are highly respected evaluations of healthcare research which produce evidence-based recommendations that are widely taken up in clinical practice and policy worldwide (*see below*).

The pulmonary rehabilitation review (10) assessed six randomised controlled trials that investigated outpatient rehabilitation begun after inpatient treatment for exacerbations. One of the six studies was our work published in the *British Medical Journal*, 2004 (1), which reported the first randomised controlled trial in the world of comprehensive early outpatient-based pulmonary rehabilitation shortly after hospital admission for acute exacerbations of COPD. The update of the review, covering July 2008 to March 2010, took in three extra studies. One of these was our work reported in *Thorax*, 2010 (2), which demonstrated, for the first time, that early pulmonary rehabilitation – in addition to improving quality of life and exercise capacity – also increased quadriceps strength and, most importantly, reduced re-admissions for exacerbations from 33% to 7% at three months.

The Cochrane review concludes that early post-exacerbation pulmonary rehabilitation is effective at reducing future hospital admissions and leads to large and clinically relevant improvements of health-related quality of life and exercise capacity (p.15). It states that one future admission is avoided for every four patients treated, and one life is saved for every six treated (p.2).

Uptake of research in national and international guidelines: This KCL work has had a significant impact on 2010 National Institute for Health and Care Excellence (NICE) guidelines on managing COPD in adults in primary and secondary care (11) (data from publication [1] is cited five times throughout). The guidelines recommend that “Pulmonary rehabilitation should be made available to all appropriate people with COPD including those who have had a recent hospitalisation for an acute exacerbation” (p.283).

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) reviews published literature and prepares an annual updated global consensus report on treatment based on scientific and clinical achievements. The 2013 report (12), translated into Italian, Japanese, Turkish and Russian and Polish to ensure wide international readership, finds that “Early outpatient pulmonary rehabilitation after hospitalisation for an exacerbation is safe and results in clinically significant improvement in exercise capacity and health status at three months” based on the findings of KCL (1) and other research. GOLD recommendations are particularly important internationally.

IMPRESS (IMPproving and Integrating RESpiratory Services), a joint initiative between the British Thoracic Society and the Primary Care Respiratory Society-UK, provides clinical leadership to the NHS to stimulate improvement and integration in respiratory services. The new IMPRESS Guide to Pulmonary Rehabilitation (2011) for commissioners and providers of pulmonary rehabilitation services (13) finds that the best evidence for the cost-effectiveness of pulmonary rehabilitation comes from four sources, one of which is Seymour 2010 (our *Thorax* paper) (2). The British Thoracic Society has just published Guidelines on Pulmonary Rehabilitation in Adults (14). These guidelines refer to our work (1,2) and recommend that "Patients hospitalised for acute

exacerbation of COPD should be offered pulmonary rehabilitation at hospital discharge to commence within one month of discharge" (p. ii3).

NHS Best Practice Guidance on Pulmonary Rehabilitation Services to commissioners across the NHS (2012) is that pulmonary rehabilitation should be offered to patients who have recently had an exacerbation requiring hospital admission (15).

Uptake of findings and cost-effectiveness in clinical care: Pulmonary rehabilitation was provided by 90% of primary care trusts in 2008, up from 64% in 2003 (16). The Department of Health (DoH) COPD Strategy Document (17) says "As identified in our Consultation Impact Assessment, ensuring the widespread use of pulmonary rehabilitation would bring annual savings of around £5.5 million a year." The DoH has convened a pulmonary rehabilitation sub-group, with representation from professional groups, people with COPD and the British Lung Foundation to advise commissioners on specifications for good quality exercise and rehabilitation services and to provide practical advice for practitioners.

5. Sources to corroborate the impact

10. Puhan MA, Gimeno-Santos E, Scharplatz M, Troosters T, Walters EH, Steurer J. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2011, Issue 10. (Reviews research findings [1,2])

National guidelines based on KCL research

11. National Institute for Health and Care Excellence (NICE) 2010. CG101 Chronic obstructive pulmonary disease (updated). Management of chronic obstructive pulmonary disease in adults in primary and secondary care. (Cites [1] pp. 652 and uses data on pp. 275,276,279,281,624,) http://www.nice.org.uk/nicemedia/live/13029/49425/49425.pdf

12. Global initiative for Chronic Obstructive Lung Disease (GOLD) 2013. Global Strategy for the Diagnosis, Management and Prevention of COPD http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf (Cites [1] p.73)

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14. British Thoracic Society Guidelines on Pulmonary Rehabilitation in Adults. Bolton CE, Bevan-Smith EF, Blakey JD, et al, *Thorax* 2013:68 ii1–ii30. (Cites [1,2,10] p.ii15)

15. National Health Service 2012. COPD Commissioning Toolkit: Pulmonary Rehabilitation Service Specification (Cites [2] p.25) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/212876/chronic-obstructive-pulmonary-disease-COPD-commissioning-toolkit.pdf

Impact on services

16. National COPD Audit 2008 reported in Nursing Times 29 September 2009, Vol. 105, No. 38 (p.15) http://www.nursingtimes.net/Journals/2013/02/08/p/z/r/090929ReviewCOPD.pdf

Consultation

17. Department of Health 2010. Consultation on a Strategy for Services for Chronic Obstructive Pulmonary Disease (COPD) in England (pp.78,118) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213840/dh_113279.pdf