

6 *COPD as an exemplar of a chronic health condition*

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Introduction

Studies suggest that around 25% of the European population receive treatment for a chronic condition. As the population ages, the prevalence of chronic diseases increases, with an average of two per person in their mid-60s and three for those surviving to their mid-70s (Barnett et al., 2012). People with chronic diseases now form a sizeable proportion of all hospital admissions both elective and emergency. Once admitted to hospital, people with multiple complex conditions may require a long length of stay and place a significant demand on acute hospital services.

Chronic obstructive pulmonary disease (COPD) is such a condition which affects between 3% and 10% of Europe's adult population and accounts for 1.1 million hospital admissions per year (Gibson et al., 2013). While it is a preventable condition, once contracted it is not curable and management strategies aim to reduce the burden of disease both on the individual and on society, which is currently estimated to cost the EU €200 billion per year (Gibson et al., 2013). Managing COPD and other long-term conditions effectively is critical not only for patients and carers but for the effective functioning of the health system itself.

In this chapter we use COPD as an exemplar of a chronic condition whose management depends on the work of the acute general hospital. As noted in Chapter 1, while the care of patients with COPD involves many specific features, it also raises issues of more general relevance to many common chronic disorders. Here we describe the burden of the disease in detail, the current management of the condition within the hospital system, and options for future care pathways illustrated by innovations that have already been implemented across a range of European health systems.

What is COPD?

Chronic obstructive pulmonary disease is an overarching term for the clinical and patho-physiological manifestations of the inflammatory response of the lungs to the repeated inhalation of noxious particles and fumes. This inflammation over time results in damage to both the airways, causing narrowing, and to the alveoli, manifesting as emphysema. People with COPD will characteristically exhibit the symptoms of cough, often with sputum production and usually worse over the winter months, with breathlessness being the most prevalent symptom (Aitsi-Selmi & Hopkinson, 2015) that tends to be progressive over time and may be accompanied by wheeze. The condition results in air-flow limitation in both the small and large airways that is detected by lung function tests, notably spirometry, which are used to confirm the diagnosis (Barnes et al., 2015). People who develop COPD probably have a genetic predisposition so that when exposed to noxious inhaled substances, most commonly cigarette smoke but also occupational dusts and, especially in low income countries, biomass fumes in poorly ventilated housing, they react with an increased inflammatory response that causes intrinsic lung damage.

The clinical course once COPD develops is variable but overall is progressive and may lead to death from respiratory failure or as a result of respiratory infection, which may cause intermittent acute exacerbations of the condition. There are a number of identifiable phenotypical expressions of the condition that provide an opportunity for delivering more personalized interventions to individuals. The one intervention that would make most difference to all those with COPD, however, is to remove the exposure to the noxious substances provoking the lung inflammation (Vestbo et al., 2013).

Additionally, co-morbidities may have a significant impact on clinical presentation and prognosis (Laforest et al., 2016) and reduced physical activity is a well recognized consequence of the condition (Hopkinson & Polkey, 2010). Accordingly, there is a need for early intervention to prevent later more severe and expensive disease.

The burden of COPD

It is difficult to provide reliable estimates about the population health burden that can be associated with COPD. This is in part because the disease is often under-diagnosed as it is not usually recognized until it is clinically apparent and moderately advanced (Lamprecht et al., 2015). Furthermore, where estimates are available, these frequently draw on varying definitions and diagnostic criteria. For example, studies of COPD prevalence have variously used self-reported respiratory symptoms, physician diagnosis of COPD, or the presence of airflow limitation with or without spirometric tests as criteria. As a consequence, available estimates vary by study design.

The recent 2010 update of the Global Burden of Disease (GBD) study revisited previous estimates on respiratory diseases and estimated the number of people to have COPD at 328 million globally (Vos et al., 2012). Worldwide the prevalence of COPD is rising, with the highest rise in the eastern Mediterranean region (119% between 1990 and 2010) and the lowest rise in Europe (22.5%), both, however, being substantial. Overall prevalence among men is around twice that of women but there are significant national variations (Adeloye et al., 2015). More recently there is evidence of falls in COPD prevalence within some western European countries, for example in Spain (Soriano et al., 2010) and Finland (Pelkonen et al., 2014), thought to be as a result of tighter tobacco controls.

COPD is one of the major causes of mortality worldwide (Figure 6.1). There has been a steady increase in mortality over time (Jemal et al., 2005) and it was estimated that COPD would become the fourth leading cause of death globally by the year 2030 (Mathers & Loncar, 2006), a projection that was confirmed by the 2010 GBD study, when COPD became the third leading cause of death globally (Lozano et al., 2012). Within Europe it is estimated to have caused 150 000 deaths in 2010, potentially rising to 338 000 a year by 2030 (Gibson et al., 2013).

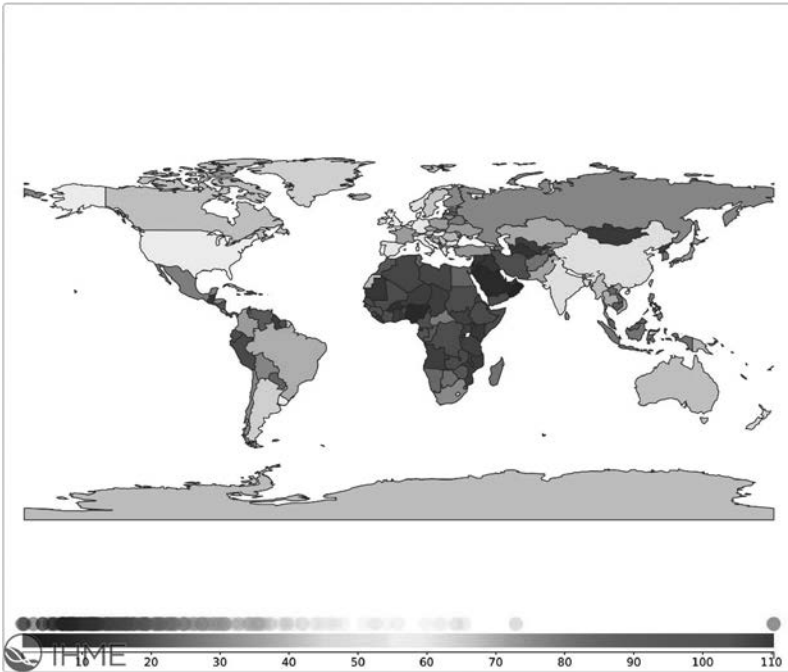


Figure 6.1 Age-standardized death rate from COPD per 100 000, both sexes, 2016

Source: Institute for Health Metrics and Evaluation, 2014

Economic costs that can be associated with the burden of COPD

As noted, COPD has been associated with considerable economic costs to the health system (Khakban et al., 2015) and projections suggest a significant further increase in direct costs by the year 2030 because of population ageing (Herse, Kilijander & Lehtimaki, 2015). COPD also poses a substantial burden at individual level in terms of activity limitation and disability and to society more broadly because of lost productivity and associated costs (Patel, Nagar & Dalal, 2014).

The predominant health care cost item is hospital utilization for exacerbations, which, in the United States in the early 2000s, was estimated to account for \$18 billion (€14 billion) annually (Anzueto, Sethi & Martinez, 2007). In southern Spain the annual cost of hospital

admissions for COPD exacerbation was estimated to be €27 million in 2000 (López-Campos Bodineau et al., 2002), with admissions to intensive care accounting for one-fifth of the total costs for COPD management (Dalal et al., 2011). Estimates of the mean actual cost per severe exacerbation range from €1711 in Greece (2006–07) (Geitona et al., 2011) to €3985 in Italy (2006) (Blasi et al., 2014). Co-morbidities such as cardiovascular disease, diabetes, asthma and anaemia (Mannino et al., 2015) were shown to further increase the economic burden that can be associated with COPD (Huber et al., 2015), as they drive increased service utilization among people with COPD (Simon-Tuval et al., 2011). With the advent of new pharmacological treatments for COPD (Barjaktarevic, Arredondo & Cooper, 2015), it is reasonable to expect that health care costs that can be associated with COPD will rise further, despite the evidence that pharmacotherapy for COPD in ambulatory care is cost-effective (Simoens, 2013). In summary, available data highlight the need to prioritize interventions aimed at delaying the progression of COPD, preventing exacerbations and reducing the risk of co-morbidities, in order to alleviate the clinical and economic burden of COPD (Wouters, 2003; Foster et al., 2006; Anzueto, Sethi & Martinez, 2007; Mannino et al., 2015).

The COPD care pathway

It is suggested that a high proportion of people with COPD remain undiagnosed either because they have few if any symptoms in the milder stages of the disease or because clinicians are slow to associate common symptoms of cough or breathlessness with the need to screen for COPD (Llordes et al., 2015). People with diagnosed COPD present usually with symptoms on the background of an exposure history, most commonly to cigarette smoke, but in around 5–15% of cases to occupational fumes, with exposure to biomass fuels a particular challenge in low and middle income countries (Smith, Mehta & Maeusezahl-Fauz, 2004). The diagnosis is made clinically but by definition it must be confirmed by spirometry lung function testing.

Once a diagnosis is made, the underlying lung damage is largely permanent and the prognosis is of a slow decline in lung function and symptoms related to the continuing exposure to the causative agent. Thus in a cigarette smoker, stopping smoking will halt further decline but not resolve any existing disease (Box 6.1).

Box 6.1 Evidence-based interventions for the management of COPD: smoking cessation

Smoking is a major risk factor for the development of COPD and current smoking is also higher among people with COPD compared to the general population, up to 47% and 20%, respectively (Schauer et al., 2014). Anthonisen et al. (1994) demonstrated that among people with early-stage COPD annual lung function decline was reduced following a smoking intervention compared to people with COPD who did not receive the intervention. There is also evidence of improvements in the presence of respiratory symptoms and quality of life over time. Against this background, smoking cessation has been proposed as an intervention with the highest impact on the natural history of COPD (Vestbo et al., 2013).

Evidence further suggests that even brief advice provided by physicians to quit smoking can significantly increase the likelihood of successfully quitting smoking (Bao, Duan & Fox, 2006; Stead et al., 2013). At the same time, while behavioural interventions (including simple advice) have modest efficacy in improving smoking quit rates among people with COPD, the combination of counselling and pharmacotherapy tends to be more effective and more cost-effective than either on its own (Hoogendoorn et al., 2010; Tashkin, 2015). International guidance recommends a five-step programme, involving brief strategies to help patients willing to quit smoking (Vestbo et al., 2013), while recognizing that more complex interventions will increase quit rates. Smoking cessation has been identified to be a cost-effective intervention for patients with COPD independently of stage of disease and should therefore be offered to every single smoking COPD patient (Buck, Richmond & Mendelsohn, 2000; Wouters, 2003).

There are no interventions other than smoking cessation that impact the natural history of the disease and arrest the decline in COPD. Management outside of smoking cessation is therefore largely designed to improve symptoms and functional status, and interventions outside smoking cessation tend to be matched to the stage of the disease and the severity of symptoms. This is further illustrated in Figure 6.2, which provides an example of a care pathway to improve outcomes in COPD.

Commissioning to improve outcomes in COPD

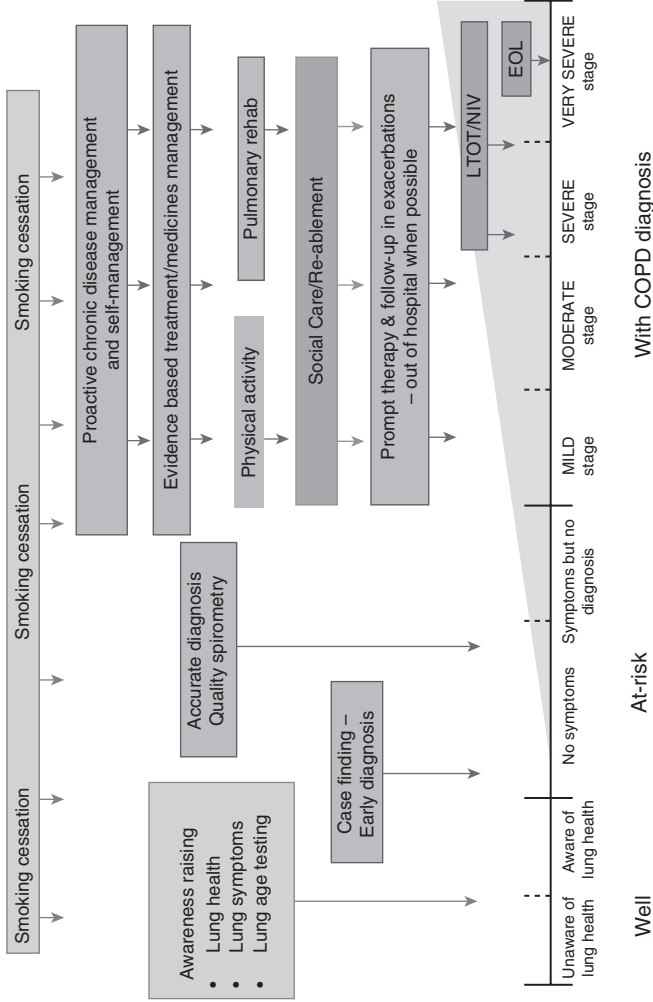


Figure 6.2 Example of a care pathway to improve outcomes in COPD

Source: Matt Kearney. Available at: <https://www.networks.nhs.uk/nhs-networks/east-of-england-respiratory-programme/key-documents/documents/Commissioning%20for%20Better%20Outcomes%20in%20COPD.pdf> (accessed 20 February 2020)

In the late stages of the disease, long-term oxygen therapy (LTOT) and non-invasive ventilatory (NIV) support may prolong life (Box 6.2) and optimizing palliative care interventions may also improve both quality and length of life. Lung transplantation in selected patients is an ultimate option in very severe COPDs, although this tends to be available to a small minority of end-stage patients only (Lane & Tonelli, 2015).

Box 6.2 Evidence-based interventions for the management of COPD: long-term oxygen therapy and non-invasive ventilatory support

Long-term oxygen therapy has been shown to prolong life in patients with COPD and chronic respiratory failure (hypoxia; deficiency of oxygen in the tissues) (Stoller et al., 2010). Effects on survival are only achieved if LTOT is given for at least 15 hours per day. LTOT is usually provided in the home environment of people with COPD. Ambulatory devices can increase the mobility of the patient and provide longer oxygen usage with resultant patient benefit (Bradley & O'Neill, 2005). Ambulatory oxygen may in some cases also reduce breathlessness on exertion in some patients who do not fulfil the strict criteria for LTOT. Providing LTOT for citizens who wish to spend time across national borders is challenging as there is no established European oxygen prescribing system and using oxygen aboard commercial flights can also be difficult and expensive with each airline following its individual set of rules.

Non-invasive ventilation (NIV) has been shown to be effective in patients with stable but very severe COPD and chronic respiratory failure (hypercapnia; high concentration of carbon dioxide in the blood), with evidence of positive effects on health status and survival (Kohnlein et al., 2014; Struik et al., 2014). NIV in acute respiratory failure in COPD due to exacerbation has been shown to positively impact respiratory acidosis, symptoms, prevalence of ventilator-associated pneumonia, and length of hospital stay (Ram et al., 2004b). Evidence suggests that NIV and invasive mechanical ventilation (IMV) are increasingly used in hospitals, primarily in emergency departments and intensive care units, and access to this therapy has been increased within recent years (López-Campos et al., 2014).

Progressive decline in lung function may lead to significant disability and quality of life impairment where palliative care interventions are most appropriate. For some people COPD leads to death; the condition accounts for around 2.5% of all deaths in Europe (Global Health Observatory, 2008). Death from respiratory causes is, however, not inevitable in COPD and a number of patients will die from linked conditions that share the same aetiology of cigarette smoking, for example heart disease and lung cancer (Zielinski et al., 1997; McGarvey et al., 2007). There is growing recognition that older patients with COPD suffer with multiple morbidities, all of which contribute to the state of frailty, that must be factored into their management. Death will more likely result from one of these diseases than it will from COPD, which in itself will be a major driver in future hospital models of care.

The effect of social factors on the outcome determinants of this complex health picture will further motivate collaboration between social and health care providers. As with many chronic diseases, the care provided to people with COPD tends to be fragmented in most system contexts. Countries are experimenting with new models of care that are designed to better meet the needs of people with long-term conditions (Nolte, Knai & Saltman, 2015), including for COPD, based on the available evidence of the (cost-)effectiveness of structured disease management of COPD (Steuten et al., 2009; Kruis et al., 2013).

The level of interaction between the patient and the hospital will depend very much upon the stage of disease of the patient, the level of support available for out-of-hospital care and the complexity of the individual case. While stable patients with COPD are typically managed outside hospital, there are a number of indications for specialist input that will require hospital care, even in those stable patients. But again these are most often delivered in the outpatient or ambulatory care setting rather than resulting in an admission to hospital. In cases where the diagnosis remains unclear or where, despite optimal treatment in primary care, a patient remains symptomatic, referral for a hospital-based specialist opinion is appropriate. In complex cases at the more severe end of the spectrum some interventions such as endoscopic lung volume reduction and surgical techniques are only available within the hospital setting (Box 6.3).

Box 6.3 Evidence-based interventions for the management of COPD: surgical treatment

Stable COPD patients with severe emphysematous lung damage (hyperinflation) can benefit from surgical treatment such as lung volume reduction surgery (LVRS). This intervention has been shown to lead, in an appropriately selected subgroup of patients with COPD, to better functional outcomes and improved survival compared to standard medical therapy (Naunheim et al., 2006). Similar to other invasive procedures, surgical treatment carries an operative mortality risk compared with medical management. The cost per quality adjusted life year (QALY) in appropriately selected individuals is estimated to be between \$40 000 and \$55 000 (Ramsey et al., 2007).

Bronchoscopic lung volume reduction (BLVR) is a novel treatment option, with clinical trials showing improvements in symptoms, exercise capacity, and lung function (Davey et al., 2015). Some countries in Europe, notably Germany and Switzerland, have now incorporated this intervention into usual clinical pathways (Pertl et al., 2014). Others are awaiting further evidence. Effective BLVR appears to be associated with a survival benefit in carefully selected patients (Hopkinson et al., 2011; Klooster et al., 2015; Garner et al., 2016; Herth et al., 2016). The cost per QALY for BLVR in that subgroup is around €25 000 (Pietzsch, Garner & Herth, 2014).

The acute exacerbation patient pathway

The main cause for a person with COPD to be admitted to hospital as an emergency will be as a result of an exacerbation of his/her condition. Exacerbations are characterized by increasing breathlessness and accompanied frequently by worsening cough and increased volume or discoloured sputum production. In many cases these acute attacks are caused by infection, while in other cases they represent a deterioration in the underlying condition worsened by atmospheric changes or other environmental factors. Exacerbations can be treated out of hospital but may also result in hospital admission; exacerbations constitute a common cause of hospitalization across Europe (Librero et al., 2016).

People admitted to European hospitals with acute COPD exacerbations have an inpatient mortality of around 4.9% and a 90 day readmission rate of 35% (Hartl et al., 2016). It is against this background that

much focus has recently been given to preventing hospital admissions (Vestbo & Lange, 2015). A number of interventions including combination therapy with inhaled corticosteroids and broncho-dilating drugs (Spencer et al., 2011), prophylactic antibiotics (Herath & Poole, 2013) and patient education with self-management (Zwerink et al., 2014) have been shown to effectively reduce exacerbation frequency and hospital admission, with evidence suggesting that these should be implemented for all patients identified to be at risk. There is less evidence that self-management with provision of “rescue packs” of antibiotics and steroid tablets in isolation of a robust education programme is effective at reducing hospital admission (Walters et al., 2010).

While it may have previously been considered that hospitals and their teams should concentrate on hospital care, it is clear that if patients are to receive a more joined-up and consistent level of care, then the influence of the hospital must extend outside of the physical bounds of the buildings themselves. There is some evidence that early self-management and proactive community interventions may reduce hospital admissions for patients with COPD at risk of exacerbation by up to a third (Effing et al., 2007; Suh, Mandal & Hart, 2013). Supporting both clinicians and patients and carers to better manage conditions to avoid unscheduled care and emergency admissions can best be facilitated by collaborative care linking to the education resources now found in abundance on the world wide web provided by national and international patient support groups (European Lung Foundation, 2013).

Which organization takes responsibility for interventions designed to reduce unscheduled care and admission to hospital will depend upon local systems but the skills and resources found in hospitals can enrich such out-of-hospital services through a variety of models. One example is the Kings Health Partners (London) Integrated Respiratory Team, which involves a partnership between hospital, community and primary care clinicians who form a collaborative team to manage out-of-hospital patients (Box 6.4). In the Spanish Ribera Salud model, a more formal vertically integrated accountable care organization directly employs an integrated community and primary team (Ribera Salud, 2016). Such integrated teams tend to be nurse-led and often include multidisciplinary members such as a physiotherapist and a social care case worker who can address the social aspects and may prevent an otherwise unnecessary admission. MDTs have been shown to be more effective at reducing admissions than nurse mono-professional teams (Wong, Carson & Smith, 2012; Kruis et al., 2013).

Box 6.4 Integrated Respiratory Team (IRT), Kings Health Partners, London, UK

The Integrated Respiratory Team works across King's College Hospital and Guy's and St Thomas' NHS Foundation Trusts and the community in London to deliver care to patients with COPD, including oxygen, pulmonary rehabilitation and supported discharge services. Key components include the IRT working in acute care hospitals to support accurate diagnosis and acute management, communication and post-discharge care, VCs in the community, a single point of referral to IRT from the community and optimizing respiratory prescribing. Respiratory virtual clinics (VCs) run twice a week in primary care. The focus of VCs is joint working between primary care teams and the IRT to systematically review the diagnosis and long-term management of the respiratory patient caseload. Since its launch in 2012 the service has seen a 34% reduction in COPD admissions and a 17% reduction in length of stay.

Source: d'Ancona et al., 2014

Intervention teams may be COPD specific or have a general remit to reduce hospital admissions across a range of patient diagnostic groups. Some are specifically targeted at reducing readmissions to hospital while others provide a prevention service for a broader range of at-risk patients identified through primary care and secondary care ambulatory services. A key enabler for effective team working, particularly across sites and organizations, and to link with the patients across a geography, is technology (see Box 6.5 below). While the evidence for primary technology-based interventions in COPD care is currently weak (Lundell et al., 2015), it seems sensible to suggest that integrated electronic patient care records, web-based self-management programmes (Luckett et al., 2016) and greater use of communication technologies to facilitate coordinated and specialist support to generalist care are to be of increasing importance in the future.

While promising, preventative services such as those described in Box 6.4 are not currently implemented widely across Europe and will therefore be available to only a minority of patients. Most patients will

be evaluated by their community-based primary care or specialist doctor and either treated or referred to the hospital. The decision-making process may be supported by (national) guidelines for the diagnosis and management of COPD that have been established in many countries (Effing et al., 2007).

Frequently, however, an acute exacerbation requires assessment in an emergency department (ED) and hospitalization. Across Europe there will be on average 200 hospital admissions for acute COPD per 100 000 population but with a 10-fold difference between countries with high and low admission rates (Gibson et al., 2013). The reasons for such variation are not known but it is hypothesized that this reflects the maturity of primary and community services, prevalence of COPD and the availability of hospital beds (Gibson et al., 2013). While much of the variation may be attributed to “system and population factors”, it seems clear that if hospitals are to moderate admissions for long-term conditions, there will be a need to extend their influence outside the physical walls of their estate.

Hospital care for exacerbations of COPD

While efforts are made to prevent admission to hospital, there is a need for severe exacerbation cases to receive the kind of management that currently can only be provided in hospital. The ideal pathway for a COPD admission can be seen to involve early triage to a specialist unit and provision of appropriate care using a MDT, to include ventilatory support where appropriate, and then discharge once safe with entry to a rehabilitation programme at an early stage following discharge (Vestbo et al., 2013). For the minority of end of life patients palliative care services should be provided (Vestbo et al., 2013).

However, hospital services are currently organized very differently across Europe, both within and between countries, which will influence the pathway for the individual COPD patient into the hospital and upon discharge. Data from the 2010–2011 European Respiratory Society audit of hospital care of people with COPD admitted to hospital with exacerbations (European COPD Audit) highlighted this variation (López-Campos et al., 2014). It showed that, for example, triage was operated in only 7% of Belgian hospitals included in the audit compared to 67% in Slovakia and 60% in Croatia. Specialist respiratory wards were available in 93% of UK hospitals but only in 27% of hospitals in

Austria. While all, or the majority, of patients in Belgium and Switzerland (90%) were seen by a nurse or physiotherapy respiratory specialist, this was only the case for 35% of patients in Poland and 20% in Turkey.

Around 5% of admissions will die in hospital, although there are now predictive tools that allow the identification of those with a much higher risk of death who are most likely to benefit from the potentially life-saving interventions of ventilator support. Respiratory acidosis is one such predictor that affects about 20% of COPD admissions and has a mortality of between 20% and 30% without assisted ventilation support. In contrast there is a significant cohort of admissions at very low risk of death who could safely be managed in the community by a MDT as described earlier. The European COPD Audit found that a considerable share of admissions is for people with mild disease (Global initiative for chronic Obstructive Lung Disease (GOLD) stage I or II), ranging from 54% admissions in Romania and 51% in Switzerland to only 35% in the United Kingdom and 30% in Turkey (López-Campos et al., 2014). This suggests that many people with COPD exacerbations currently admitted to hospital could potentially be managed in the community if appropriate services (such as MDTs) were available. In contrast, patients requiring ventilatory support, or who are at risk of developing ventilatory failure requiring such support, should be managed in hospital according to national and international management guidelines. Yet, as data from the European COPD Audit indicate, availability of high dependency units that deliver ventilatory support varies substantially across countries, from 95% of Swiss hospitals to only 22% in Greece and 10% in Romania. Non-invasive ventilation was provided in all hospitals in Switzerland, Ireland and Slovakia but only in 70% of Croatian and 60% of Romanian units. For some patients the key hospital intervention can be palliative and end of life care, yet in the audit this service was available in only 13% of Greek hospitals and 5% in Turkey compared with 91% in Ireland and 92% in the United Kingdom.

Furthermore, the European COPD Audit found that hospital adherence to the 2010 GOLD standards varied considerably both within and across countries (Roberts et al., 2013). Spirometric confirmation of diagnosis was available in just 59% of cases, while even in patients with previous admissions with the same diagnosis 37% had no record of lung function confirmed diagnosis. Further more, of those with a

spirometry result recorded, 13% had a result incompatible with the diagnosis of COPD. Taking arterial blood gases on admission, which provides essential information about prognosis and the need for key interventions, was performed in 91.5% cases with an interquartile range (IQR) between hospitals of 78.4% and 98.7% and an IQR between countries of 81.9% and 93.5% (Table 6.2).

As indicated above, diversity of pathways, if not quality of care, for people with COPD admitted to hospital with exacerbations across different health systems is in part the consequence of the different organizational structures that are based on medical models rather than population need. For example, the hospital infrastructure in many countries distinguishes smaller local units and larger regional institutions that are often associated with a university and thus include teaching and research functions. A small number of European countries operate a national respiratory centre of excellence, such as Romania and Slovakia, while elsewhere expertise is spread among several tertiary institutions, including in Spain and the United Kingdom (López-Campos et al., 2014). The resources and organization of care vary widely, with larger hospitals tending to have a higher number of specialist doctors and offering a wider range of specialist services while not necessarily providing better quality care to patients or improving patient outcomes (López-Campos et al., 2014) (Table 6.1).

Care experiences and standards of care that people with COPD in European countries can expect when admitted with a COPD exacerbation will depend very much on the particular hospital they present to. Data from both the European and UK audits of hospital COPD care suggest that the number of specialists per 1000 beds is the single most important resource factor in determining outcomes for patients (Hartl et al., 2016; Price et al., 2006).

Data further suggest that current service delivery often falls short of international guideline standards and that there is major variation in quality of care not just between countries but equally within them (Table 6.2).

Post-acute care

There is growing recognition that the hospital has potential to influence out-of-hospital care not just to prevent admission but also to prevent

Table 6.1 Selected characteristics of hospital centres participating in the 2010–11 European COPD Audit Variation

| Country | Number of hospital centres participating | Median number of beds per hospital (10th, 90th percentile) | Median catchment population (10 000s) per unit (10th, 90th percentile) | Number of respiratory specialist doctors per unit (10th, 90th percentile) |
|---------------------|--|--|--|---|
| Austria | 47 | 377 (169–1 098) | 10.6 (2.87–25) | 7 (3–12) |
| Belgium | 21 | 450 (240–935) | 20 (6–100) | 5 (3–12) |
| Croatia | 8 | 461 (105–1 191) | 34 (11–75) | 7 (2–13) |
| Greece | 22 | 575 (200–700) | 32.5 (6–15) | 5 (2–6) |
| Republic of Ireland | 11 | 343 (131–851) | 25 (12–50.6) | 2 (1–6) |
| Malta | 1 | 850 | 41.8 | 5 |
| Poland | 38 | 400 (182–1 002) | 25 (5.8–21) | 6 (2–16) |
| Romania | 9 | 185 (118–517) | 47.5 (17–77) | 11 (7–21) |
| Slovakia | 3 | 644 (400–887) | 106 (12–200) | 7 (2–11) |
| Spain | 91 | 460 (150–1 023) | 25 (3.7–99.9) | 8 (3–16) |
| Switzerland | 18 | 245 (161–784) | 15 (3.5–40) | 3 (1–6) |
| Turkey | 20 | 610 (133–1 200) | 100 (9.6–1 000) | 6 (3–14) |
| United Kingdom | 112 | 527 (290–1 000) | 30 (17–55) | 4 (2–8) |

Source: López-Campos et al., 2014

Table 6.2 *Quality of COPD care across European hospitals against recommendations of the GOLD strategy document*

| Audit standard | Compliance at case level (%) | Absolute case numbers | Median by hospital (%) | IQR by hospital (%) | Median by country (%) | IQR by country (%) |
|--|-------------------------------------|------------------------------|-------------------------------|----------------------------|------------------------------|---------------------------|
| Spirometry result available at admission | 59.4 | 9 513/16 018 | 63.1 | 43.4–83.3 | 64.7 | 49.3–69.9 |
| Arterial blood gas performed at admission | 82.4 | 13 191/16 018 | 91.5 | 78.4–98.7 | 88.1 | 81.9–93.5 |
| Chest radiograph performed at admission | 98.6 | 15 790/16 018 | 100 | 98.6–100 | 99.0 | 98.0–99.4 |
| Controlled oxygen therapy used | 84.9 | 13 602/16 018 | 89.7 | 76.9–97.9 | 85.7 | 79.8–88.5 |
| Short-acting bronchodilator use | 91.1 | 14 594/16 018 | 95.9 | 89.1–100 | 91.4 | 80.3–94.7 |
| Non-use of intravenous methylxanthines | 85.7 | 13 742/16 018 | 96.8 | 83.3–96. | 79.9 | 54.7–97.4 |
| Systemic corticosteroids given | 82.3 | 13 187/16 018 | 87.9 | 77.3–95.0 | 76.9 | 62.7–88.3 |
| Antibiotics given if sputum purulence or IMV | 90.5 | 8 457/9 347 | 93.5 | 85.7–100 | 89.5 | 86.3–93.6 |
| NIV given if pH <7.35 and PaCO ₂ >6 kPa | 51.0 | 1 133/2 222 | 58.6 | 40–77.8 | 47.0 | 40.9–66.6 |
| IMV given if pH <7.25 and PaCO ₂ >8 kPa | 15.4 | 73/473 | 50.0 | 33.3–100 | 31.6 | 22.2–44.4 |
| Fulfilled all 10 recommendations | 15.3 | 2 444/16 018 | 16.6 | 9.09–25.0 | 10.1 | 5.18–17.8 |

Source: Roberts et al., 2013

readmission and there are excellent examples of where such influence has major benefits to the patient and to the system. Once a patient has recovered from their acute illness they are usually discharged back to the environment they came from, such as the community or their own home. In some cases, the deterioration in their condition will not have improved enough to allow this to happen and in some health systems a period of convalescence or rehabilitation may be arranged. In other cases this is not an option and a patient may be placed within institutional care, such as residential care or a nursing home. Available evidence supports the use of ESD for selected patients with acute exacerbation of COPD as an effective and safe intervention (Echevarria et al., 2016). Such schemes aim to accelerate discharge from hospital with the provision of continued support in a community setting, typically at the same intensity that would have been provided had the patient remained in hospital, and involving MDTs to prevent (re)admissions. Although countries are increasingly introducing these type of programmes, their availability varies considerably. For example, the European COPD Audit found that 75% of participating UK hospitals offered early discharge support programmes compared to only 37% in Switzerland, the next most frequent user. In many of the participating countries there was no use of such programmes (López-Campos et al., 2014). This suggests that many patients may be receiving suboptimal care.

There are also concerns about the transition from hospital to community, with patient experience varying both within and between countries. This ranges from simple discharge from hospital without coordination of care post discharge to that of an integrated care system where there is seamless continuity of care with a single organization responsible for both secondary and primary care services with a shared electronic health record (Ribera Salud, 2016). Telehealth may offer opportunities to link the hospital to the patient after discharge and to provide monitoring to ensure clinical improvement but also to then provide early warning signs of a deterioration that initiates an early intervention to prevent readmission (Box 6.5), with telemedicine considered more broadly as an aid to the management of long-term conditions (McKinstry, Pinnock & Sheikh, 2009; Hernandez, Mallow & Narsavage, 2014). However, rigorous evaluation is required as in other areas of medicine it has often failed to live up to what has been promised.

Box 6.5 Telehealth teams for monitoring patients with COPD post discharge, Barcelona, Spain

As part of the EU-funded Supporting Healthier and Independent Living for Chronic Patients and Elderly (NEXES), a multidisciplinary telehealth team was established in one of the four health sectors of the city of Barcelona, Spain, to monitor post COPD exacerbation discharge patients. Patients were monitored remotely and had access to regular video conferencing, a dedicated call centre and an online patient management web portal. The call centre was managed by a health coach who might deal with problems directly or refer to the patient's case manager who in turn could access other services as required, including the GP, other health care professionals or a respiratory specialist depending upon the issue identified. The intervention was associated with significantly fewer hospitalizations among patients with chronic respiratory diseases, reduced in-hospital days for patients in a Home Hospitalization/Early Discharge scheme, and increased quality of monitoring of patients receiving additional support.

Source: Hernandez et al., 2015

Where care provision remains fragmented, alternative approaches to providing more joined-up care include a discharge bundle quality improvement tool (Box 6.6), which promotes a standardized set of processes designed to enhance optimal transition back to the community (Turner, 2015) and which has been shown to reduce emergency readmission to hospital post discharge (Hopkinson et al., 2012).

Box 6.6 COPD discharge care bundle project, London, UK

A care bundle is a structured way of improving the processes of care and patient outcomes. It involves a small set of between three and five evidence-based practices that, when performed collectively and reliably, have been shown to improve patient outcomes. The project involved the design and implementation of a COPD discharge care

Box 6.6 (cont.)

bundle in northwest London. The bundle includes: (i) smoking cessation advice; (ii) assessment and referral for post-discharge pulmonary rehabilitation; (iii) patient education and self-management plans; (iv) medication review including inhaler technique checks; and (v) assured follow-up post discharge. Evidence from the initial implementation phase suggested that the introduction of the care bundle had reduced readmission rates and improved both staff and patient satisfaction with the discharge process. Further evaluation of the subsequent roll-out of the care bundle to other acute hospitals in London provided further evidence that the introduction of the bundle was associated with a reduction in readmission rates (Lavery et al., 2015).

Source: Hopkinson et al., 2012

Other interventions that can reduce readmission rates and which lie within the influence of the hospital include early pulmonary rehabilitation (Puhan et al., 2011), while for those with end-stage disease, and a high chance of relapse, advanced care planning may result in the avoidance of future admissions. Evidence suggests that in those cases care provided in the patient's own home or in a community setting that is more suited to end of life care can be effective in reducing the symptom burden for patients (Gomes et al., 2013).

Rehabilitation

As noted above, pulmonary rehabilitation has been shown to be a very cost-effective therapy in COPD (Spruit et al., 2013; McCarthy et al., 2015). Reported benefits include improved exercise capacity and quality of life, reduced symptoms, anxiety and depression, and enhanced medication effects. Rehabilitation has further been shown to reduce hospitalizations and length of hospital stay as well as improving the recovery after hospitalization because of COPD exacerbation (Puhan et al., 2016). Components of pulmonary rehabilitation can vary but a comprehensive programme typically includes smoking cessation, exercise training, nutrition therapy, and patient education. Programmes are designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term

adherence to health-enhancing behaviours. The collaborative approach of multiple provider services working across organizational boundaries to provide rehabilitation at its best can have much wider system impacts as exemplified by the Copenhagen SIKS programme (Box 6.7), which has become a model for locality-based integrated care systems in Denmark (Jacobsen et al., 2014).

Box 6.7 Integrated effort for people living with chronic diseases (SIKS) project, Copenhagen, Denmark

Set up as a research project for the period 2005–2007, the SIKS project focused on the implementation of rehabilitation programmes for people with type 2 diabetes, COPD, and heart disease or with balance problems following falls, requiring close collaboration between a local health care centre, a local hospital, and GPs. Standard packages of rehabilitation included disease-specific education and patient self-management sessions, a physical training session, nutritional consultation sessions and smoking cessation programmes. The programmes lasted 7–12 weeks depending on the specific disease. Patients were followed up upon completion of the programme. An evaluation of the impact of rehabilitation on health-care utilization found that compared with their matched controls, patients with COPD participating in the programme in the health care centre showed smaller increases in hospital admissions, bed days and outpatient visits over a two-year period that were statistically significant (at 18%, 34%, and 24%, respectively). The SIKS project is reported to have influenced the way integrated care has been conceptualized in Denmark. For example, after completion of the project, health care centres based on the SIKS model were established across Denmark and the experiences informed wider policy development for coordinated care approaches in Denmark.

Source: Jacobsen et al., 2014

Despite its demonstrable benefits, rehabilitation after an exacerbation is not widely offered in Europe and elsewhere. Data from the European COPD Audit showed that in 2010–11 pulmonary rehabilitation at discharge was available in just half of participating hospitals, ranging

from 91% in Ireland and 88% in the United Kingdom to just 18% in Austria and 20% in Romania (López-Campos et al., 2014). Also drawing on the European COPD Audit and additional data, Spruit et al. (2014) reported large differences among pulmonary rehabilitation programmes in mostly high income countries in Europe and North America as they relate to the setting, composition of the pulmonary rehabilitation team, methods of referral and types of reimbursement, among others. For example, in North America the majority of programmes (~70%) were delivered in outpatient settings whereas in European countries this was the case for half of the programmes while another 30% were offered in both inpatient and outpatient settings. There was also substantial heterogeneity in referral practices, in terms of the types of practitioners who refer patients and the types of patients referred, which was attributed, in part, to varying knowledge, attitudes, and perceptions of pulmonary rehabilitation within and across countries, and which may impact on patient outcomes. Importantly, the survey found that only a small number of patients were enrolled in pulmonary rehabilitation across the centres studied, highlighting that a potentially large number of people with potential to benefit from pulmonary rehabilitation are either not referred, not enrolled, lack access, or choose not to participate (Rochester & Spanevello, 2014).

Workforce

The workforce required to staff the future European hospitals will need to meet the challenges posed by advances in medical innovation and technology, the changing population needs as reflected by older people with complex multiple chronic conditions, but most of all by the impending shortages of clinical staff. While there is no European standard for what constitutes an ideal hospital staffing level to make such a judgement, evidence from large-scale studies suggests that higher numbers of doctors and of nurses per hospital bed correlate with better outcomes for patients (Needleman et al., 2011; Hartl et al., 2016). For example, using data from the European COPD Audit, Hartl et al. (2016) found that a higher number of respiratory specialists per 1000 beds reduced the risk of post-discharge mortality for patients with COPD. As we have noted above, the European and UK/England and Wales COPD Audits highlight not only large variations in clinical staff per 1000 beds between countries but also within each country (López-Campos et al.,

2014; Stone et al., 2015). This suggests that workforce distribution is not necessarily based upon workload or patient need but is dependent upon other factors that might include local funding, hospital status or specialty and academic interest, geography and social factors, or simply historical models of care.

The optimal management of patients with COPD faces the same challenges as the health care sector does more widely in deploying an appropriately trained workforce, with shortages in some medical specialties, and especially nurses, alongside demographic changes. Countries are experimenting with extended and new roles for nurses in particular to support nurses and physicians working within the hospital system. Such roles include physician associates with a science-based first degree plus a vocational master's degree who are trained to perform a number of duties, including taking medical histories, performing examinations, diagnosing illnesses, analysing test results, and developing management plans. They are supervised by a senior doctor but take on many of the more routine duties that a physician might otherwise fulfil. Respiratory nurses or physiotherapy specialists are independent practitioners with master's level or equivalent training in respiratory medicine and often specifically in COPD care. They may be deployed as part of a hospital or joint community team bridging the gap between hospital and community care with in-reach or outreach connectivity. They may lead a multiprofessional team with or without medical input. Key roles are within supported discharge, admission prevention teams and pulmonary rehabilitation. The exercise physiologist is a professional role developed in the United States and now adapted in some European systems. They usually hold a biomedical sciences degree with an additional master's qualification in exercise physiology, and specializing further in the management of people with chronic conditions, notably heart and lung disease. Exercise physiologists may prescribe and oversee a personalized exercise programme for patients with COPD and may also supervise a pulmonary rehabilitation programme for a larger number of patients with COPD. The ability to plan and oversee tailored exercise programmes raises the potential to extend rehabilitation to those with co-morbidities with perhaps greater confidence than staff trained purely in COPD or respiratory health care. The result is a blurring of traditional responsibilities in an attempt to provide a wider professional team contributing to a competencies-based workforce. The benefits of this trend include a refocusing of roles around the needs of the patient

today rather than to continue a pattern of service delivery configured decades in the past, and to provide multiskilled staff who can meet most of the patient's needs in a single episode of care rather than requiring multiple professionals to input multiple narrow specialized interactions.

COPD teams have been at the forefront of developing new professional roles but there is little consistency of adoption across Europe. The aforementioned European COPD Audit report found that at the time of the study participating hospitals in several countries did not have specialist respiratory trained physiotherapists (Romania, Spain, Turkey), or nurse specialists (Austria, Poland, Switzerland) and while all countries recognized respiratory function technicians as a team member, they were not employed in all hospitals (Roberts et al., 2013). Even where there are roles with similar titles, their competencies and scope are often difficult to compare because of differences in training, and the clinical systems within which they operate.

Specialist resources

There is no equivalence across Europe in terms of function and size or resource level for hospitals that establishes either a minimum or optimum standard, although there are standards described within international COPD recommendations for the interventions that should be available to patients admitted to hospital with exacerbations of COPD (GOLD, 2017). The patient might reasonably expect to receive the same high quality care wherever they present, accepting that this might not be all provided in one location. A range of factors will determine what can be provided, ranging from geography and accessibility to workforce availability and financial pressures on resource allocation. Within any one country, however, systems that share data and promote real-time interaction between clinicians working separately have the potential to reduce the variation in quality of care that is currently the reality. Life-saving treatments can be administered if patients are appropriately diagnosed and triaged in terms of severity using history taking and clinical examination followed by basic blood tests, arterial blood gas measurement and a chest radiograph which should be available at all hospital sites. Severely ill patients with acute respiratory acidosis need to have access to ventilatory support within a period of 1 to 3 hours of presentation according to management guideline recommendations (Celli, MacNee & ATS/ERS Task Force, 2004; Vestbo et al., 2013). This

is one key and potentially life-saving intervention outside the basic level of care that can be provided in all locations, i.e. antibiotics, steroids, bronchodilators and oxygen therapy. NIV, while currently often delivered by respiratory specialists, is also managed in some countries by anaesthetists, and some services are led by specialist nurses or physiotherapists who could be supported remotely by specialist doctors if not available on site (Bierer & Soo Hoo, 2009; Pinto et al., 2010; Cabrini et al., 2015; Ambrosino et al., 2016). Invasive ventilation required for those who fail on non-invasive support or where there are other factors making this the more appropriate intervention is more complex and is nearly always delivered by anaesthetic-trained staff in an intensive care unit setting. Ideally such facilities – i.e. the equipment, monitoring facilities, the staff and the specialist unit – should be available in every hospital admitting COPD exacerbations or be accessible by rapid site transfer. This is not the case at present (Roberts et al., 2013; López-Campos et al., 2014).

For the subacute situation all hospitals should also provide diagnostic facilities available to hospital, primary care and community physicians that will ensure accurate diagnosis of COPD. These would include lung function testing and imaging, notably chest radiography and CT scanning. Advice from an expert clinician would be helpful in making the more difficult diagnostic cases where other conditions may exist as co-morbidities or as differential diagnoses.

Stable patients at the advanced stage of the disease will require more complex investigation and interventions that may include LVRS and potentially, in a very small number of cases, lung transplantation. Such patients would be referred to a specialist centre with specific expertise in these techniques and with the expensive equipment and clinical staff available. Once again the implementation of technological solutions would provide opportunities for patients in this situation to be considered regardless of their physical location by the transmission of images, electronic patient records and by video interviews between clinicians and patients. In this manner a hub and spoke model provides an efficient and effective use of resources.

In summary, a technological interconnectivity of hospitals provides an opportunity for all patients to access specialty opinions regardless of their location and situation. Critical to good patient care will be establishing the correct diagnosis at an early stage and, for patients admitted to hospital, early access to assisted ventilation if needed and

then prior to discharge a comprehensive care package that will reduce the progression of the disease and risk of further admission. A small number of highly specialized units could provide nationally available expertise to all while networked to a larger number of more local provider units. These in turn, or through the national specialty units, could also provide networked support to both primary care health professionals and to patients and carers facilitated by technological solutions.

Barriers to delivering optimal care

Optimal care can be defined as a composite of evidence-based and consensus-based interventions that promote good outcomes for patients, and guidelines, or in a resource-constrained system might more productively be considered as the appropriate implementation of these interventions within a value-based hierarchy. Unlike for most chronic medical conditions, this value-based approach is well documented for COPD and it provides a useful reminder to clinicians of their responsibilities to the system as well as to the patient (Figure 6.3).

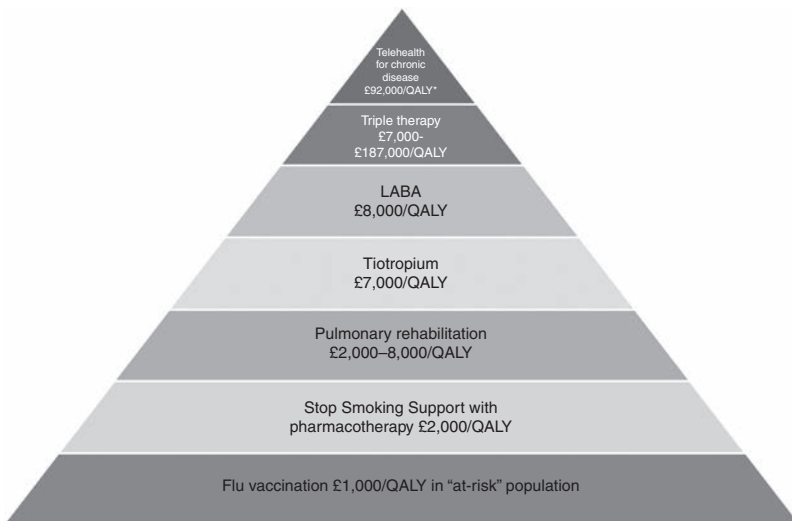


Figure 6.3 The pyramid of value for COPD interventions

Source: IMPRESS Guide to the relative value of COPD interventions (2012). British Thoracic Society Reports, Vol. 4, Issue 2. ISSN 2040-2023.

Implementing optimal care is a multifaceted challenge with the need to modify clinical behaviours and a culture that requires a shift in the balance of control towards patients and away from clinicians. The European evidence relating to the quality of care offered by hospitals confirms that the complex interactions that constitute an organization account for the majority of the variation between units (Ruparel et al., 2016). The principle of value to the system is equally valid when applied to a hospital as it is to the care offered to an individual patient. The evidence that resource-rich organizations perform better in delivering high quality COPD care is relatively weak and although there are some associations between medical staffing levels and better care outcomes (Roberts et al., 2013; Hartl et al., 2016), there is no direct evidence of a link with other inputs. However, it is concerning that European audits reveal that some elements of treatment that have been shown to benefit patients with COPD are unavailable in many of the hospitals that care for these patients.

A useful example of the complex organizational interactions that account for some unwarranted variations in care is the degree to which specialist COPD care is offered to patients within any institution. Much care of patients with COPD in hospitals is delivered by non-respiratory specialists and the evidence is that generalists are less likely to deliver optimum COPD care to their patients with COPD (Hosker et al., 2007; López-Campos et al., 2015). At a population level, most COPD care is delivered out of hospital by generalists, while most of the expertise remains locked within hospital buildings. Providing greater access to that expertise both within and outside the hospital is an important facet of delivering optimal care. Sadly, patients themselves are unlikely to understand what good care looks like and are therefore unlikely to be able to negotiate high quality care with their health teams. Better-informed patients might drive better COPD care.

Until regular measurement of care quality becomes a routine element of clinical care it remains difficult to identify areas of excellence or those where improvement is required. Engaging clinicians in reviewing performance data is a key challenge but if successful promotes the improvement of clinical practice (Flottorp et al., 2010). Leadership is required if Europe is to move forward in redesigning hospital care for patients with COPD. That must come from the health professions and from politicians. At present, there is no functional European health profession voice to provide that leadership and little evidence of a united political will.

COPD and the future hospital – summary

The hospital of the future is likely over time to be admitting sicker and frailer patients with COPD exacerbations. The evidence for ambulatory care as an alternative to admission (Ram et al., 2004a) and early discharge once admitted is compelling (Echevarria et al., 2016) but will not be appropriate for all individuals who require a greater level of support. Particularly in health systems with under-developed primary care, these measures offer huge potential benefits to hospitals in the future. Such a hospital would be a central hub, supported by technology that could provide a learning and education resource supporting patient self-management (Smidth et al., 2013) for a large population, over a geographical area well beyond its historical area of influence. Patients at risk of acute deterioration and admission could be directly linked to a COPD clinical monitoring team to provide the opportunity for early interventions to improve patient well-being (McLean et al., 2011). Patients would be managed at distance, gaining specialist expertise without the need to regularly travel to hospital appointments (D’Ancona et al., 2014). Clinicians too could be connected using digital communication, sharing patient clinical records, laboratory results, and imaging, and holding multidisciplinary discussions with colleagues via video conferencing and email to provide wider access to expertise extending well outside the physical buildings of the hospital itself. The challenge has always been how to provide equality of access to higher standards of care regardless of geography. Providing a technological network of the highest level of expertise available to all provides an opportunity to make progress towards that ideal while managing more people in an out-of-hospital setting.

References

- Adeloye D et al. (2015). Global and regional estimates of COPD prevalence: systematic review and meta-analysis. *J Glob Health*, 5:020415.
- Aitsi-Selmi A, Hopkinson NS (2015). Breathlessness, physical activity and sustainability of healthcare. *Eur Respir J*, 45:284–5.
- Ambrosino N et al. (2016). Tele-monitoring of ventilator-dependent patients: a European Respiratory Society Statement. *Eur Respir J*, 48(3):648–63. doi: 10.1183/13993003.01721-2015. Epub 7 Jul 2016.

- Anthonisen NR et al. (1994). Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. *JAMA*, 272:1497–505.
- Anzueto A, Sethi S, Martinez FJ (2007). Exacerbations of chronic obstructive pulmonary disease. *Proc Am Thorac Soc*, 4:554–64.
- Bao Y, Duan N, Fox SA (2006). Is some provider advice on smoking cessation better than no advice? An instrumental variable analysis of the 2001 National Health Interview Survey. *Health Serv Res*, 41:2114–35.
- Barjaktarevic IZ, Arredondo AF, Cooper CB (2015). Positioning new pharmacotherapies for COPD. *Int J Chron Obstruct Pulmon Dis*, 10:1427–42.
- Barnes PJ et al. (2015). Chronic obstructive pulmonary disease. *Nat Rev Dis Primers*, 1:15076.
- Barnett K et al. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet*, 380:37–43.
- Bierer GB, So Hoo GW (2009). Noninvasive ventilation for acute respiratory failure: a national survey of Veterans Affairs hospitals. *Respir Care*, 54(10):1313–20.
- Blasi F et al. (2014). The clinical and economic impact of exacerbations of chronic obstructive pulmonary disease: a cohort of hospitalized patients. *PLoS One*, 9:e101228.
- Bradley JM, O'Neill B (2005). Short-term ambulatory oxygen for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 4:CD004356.
- Buck DJ, Richmond RL, Mendelsohn CP (2000). Cost-effectiveness analysis of a family physician delivered smoking cessation program. *Prev Med*, 31:641–8.
- Cabrini L et al. (2015). An international survey on noninvasive ventilation use for acute respiratory failure in general non-monitored wards. *Respir Care*, 60(4):586–92. doi: 10.4187/respcare.03593. Epub 18 Nov 2014.
- Celli BR, MacNee W, ATS/ERS Task Force (2004). Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*, 23:932–46.
- D'Ancona G et al. (2014). P29 Impact of Respiratory Virtual Clinics in Primary Care on Responsible Respiratory Prescribing and Inhaled Corticosteroid Withdrawal on Patients with COPD: a Feasibility Study. *Thorax*, 69:A90.
- Dalal AA et al. (2011). Costs of COPD exacerbations in the emergency department and inpatient setting. *Respir Med*, 105:454–60.

- Davey C et al. (2015). Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HiFi study): a randomised controlled trial. *Lancet*, 386:1066–73.
- Echevarria C et al. (2016). Early Supported Discharge/Hospital at Home for Acute Exacerbation of Chronic Obstructive Pulmonary Disease: a Review and Meta-Analysis. *COPD*, 13:523–33.
- Effing T et al. (2007). Self-management education for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 4:CD002990.
- European Lung Foundation (2013). *Lung Health in Europe. Facts and Figures*. United Kingdom, European Lung Foundation.
- Flottorp SA et al. (2010). *Using audit and feedback to health professionals to improve the quality and safety of health care*, Copenhagen, WHO Regional Office for Europe.
- Foster TS et al. (2006). Assessment of the economic burden of COPD in the U.S.: a review and synthesis of the literature. *COPD*, 3:211–18.
- Garner J et al. (2016). Survival after Endobronchial Valve Placement for Emphysema: A 10-Year Follow-up Study. *Am J Respir Crit Care Med*, 194:519–21.
- Geitona M et al. (2011). The cost of COPD exacerbations: a university hospital-based study in Greece. *Respir Med*, 105:402–9.
- Gibson GJ et al. (2013). Respiratory health and disease in Europe: the new European Lung White Book. *Eur Respir J*, 42:559–63.
- Global Health Observatory (2008). *Causes of death in 2008* (Online). World Health Organization. Available at: http://www.who.int/gho/mortality_burden_disease/causes_death_2008/en/ (accessed 9 December 2016).
- GOLD (2017). Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease. Available at: <http://goldcopd.org> (accessed 2 February 2020).
- Gomes B et al. (2013). Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers. *Cochrane Database Syst Rev*, 6:CD007760.
- Hartl S et al. (2016). Risk of death and readmission of hospital-admitted COPD exacerbations: European COPD Audit. *Eur Respir J*, 47:113–21.
- Herath SC, Poole P (2013). Prophylactic antibiotic therapy for chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev*, 11:CD009764.
- Hernandez C, Mallow J, Narsavage GL (2014). Delivering telemedicine interventions in chronic respiratory disease. *Breathe (Sheff)*, 10:198–212.

- Hernandez C et al. (2015). Integrated care services: lessons learned from the deployment of the NEXES project. *Int J Integr Care*, 15:e006.
- Herse F, Kiljander T, Lehtimäki L (2015). Annual costs of chronic obstructive pulmonary disease in Finland during 1996–2006 and a prediction model for 2007–2030. *NPJ Prim Care Respir Med*, 25:15015.
- Herth FJ et al. (2016). Endoscopic Lung Volume Reduction: An Expert Panel Recommendation. *Respiration*, 91:241–50.
- Hoogendoorn M et al. (2010). Long-term effectiveness and cost-effectiveness of smoking cessation interventions in patients with COPD. *Thorax*, 65:711–18.
- Hopkinson NS, Polkey MI (2010). Does physical inactivity cause chronic obstructive pulmonary disease? *Clin Sci (Lond)*, 118:565–72.
- Hopkinson NS et al. (2011). Atelectasis and survival after bronchoscopic lung volume reduction for COPD. *Eur Respir J*, 37:1346–51.
- Hopkinson NS et al. (2012). Designing and implementing a COPD discharge care bundle. *Thorax*, 67:90–2.
- Hosker H et al. (2007). Variability in the organisation and management of hospital care for COPD exacerbations in the UK. *Respir Med*, 101(4):754–61. Epub 11 Oct 2006.
- Huber MB et al. (2015). Excess costs of comorbidities in chronic obstructive pulmonary disease: a systematic review. *PLoS One*, 10:e0123292.
- Institute for Health Metrics and Evaluation (2014). Web site. Available at: <http://www.healthdata.org/> (accessed 20 February 2020).
- Jacobsen R et al. (2014). The effect of rehabilitation on health-care utilisation in COPD patients in Copenhagen. *Clin Respir J*, 8(3):321–9. doi: 10.1111/crj.12074. Epub 23 Dec 2013.
- Jemal A et al. (2005). Trends in the leading causes of death in the United States, 1970–2002. *JAMA*, 294:1255–9.
- Khakban A et al. (2015). Ten-Year Trends in Direct Costs of COPD: A Population-Based Study. *Chest*, 148:640–6.
- Klooster K et al. (2015). Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation. *N Engl J Med*, 373:2325–35.
- Kohnlein T et al. (2014). Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med*, 2:698–705.
- Kruis AL et al. (2013). Integrated disease management interventions for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 10:CD009437.

- Laforest L et al. (2016). Frequency of comorbidities in chronic obstructive pulmonary disease, and impact on all-cause mortality: a population-based cohort study. *Respir Med*, 117:33–9.
- Lamprecht B et al. (2015). Determinants of underdiagnosis of COPD in national and international surveys. *Chest*, 148:971–85.
- Lane CR, Tonelli AR (2015). Lung transplantation in chronic obstructive pulmonary disease: patient selection and special considerations. *Int J Chron Obstruct Pulmon Dis*, 10:2137–46.
- Laverty AA et al. (2015). Impact of a COPD discharge care bundle on readmissions following admission with acute exacerbation: interrupted time series analysis. *PLoS One*, 10(2):e0116187. doi: 10.1371/journal.pone.0116187.
- Librero J et al. (2016). Trends and area variations in Potentially Preventable Admissions for COPD in Spain (2002–2013): a significant decline and convergence between areas. *BMC Health Serv Res*, 16:367.
- Llordes M et al. (2015). Prevalence, Risk Factors and Diagnostic Accuracy of COPD Among Smokers in Primary Care. *COPD*, 12:404–12.
- López-Campos JL et al. (2014). Variability of hospital resources for acute care of COPD patients: the European COPD Audit. *Eur Respir J*, 43(3):754–62. doi: 10.1183/09031936.00074413.
- López-Campos JL et al. (2015). Antibiotic Prescription for COPD Exacerbations Admitted to Hospital: European COPD Audit. *PLoS One*, 10(4):e0124374. doi: 10.1371/journal.pone.0124374.
- López-Campos Bodineau JL et al. (2002). [Analysis of admissions for chronic obstructive pulmonary disease in Andalusia in 2000]. *Arch Bronconeumol*, 38:473–8.
- Lozano R et al. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380:2095–128.
- Luckett T et al. (2016). Content and quality of websites supporting self-management of chronic breathlessness in advanced illness: a systematic review. *NPJ Prim Care Respir Med*, 26:16025.
- Lundell S et al. (2015). Telehealthcare in COPD: a systematic review and meta-analysis on physical outcomes and dyspnea. *Respir Med*, 109:11–26.
- McCarthy B et al. (2015). Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 2:CD003793.
- McGarvey LP et al. (2007). Ascertainment of cause-specific mortality in COPD: operations of the TORCH Clinical Endpoint Committee. *Thorax*, 62:411–15.

- McKinstry, B, Pinnock H, Sheikh A (2009). Telemedicine for management of patients with COPD? *Lancet*, 374:672–3.
- McLean S et al. (2011). Telehealthcare for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 7:CD007718.
- Mannino DM et al. (2015). Economic Burden of COPD in the Presence of Comorbidities. *Chest*, 148:138–50.
- Mathers CD, Loncar D (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*, 3:e442.
- Naunheim KS et al. (2006). Long-term follow-up of patients receiving lung-volume-reduction surgery versus medical therapy for severe emphysema by the National Emphysema Treatment Trial Research Group. *Ann Thorac Surg*, 82:431–43.
- Needleman J et al. (2011). Nurse staffing and inpatient hospital mortality. *N Engl J Med*, 364:1037–45.
- Nolte E, Knai C, Saltman RB (2015). *Assessing chronic disease management in European health systems: concepts and approaches*. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory for Health Systems and Policies
- Patel JG, Nagar SP, Dalal AA (2014). Indirect costs in chronic obstructive pulmonary disease: a review of the economic burden on employers and individuals in the United States. *Int J Chron Obstruct Pulmon Dis*, 9:289–300.
- Pelkonen MK et al. (2014). Twenty-five year trends in prevalence of chronic bronchitis and the trends in relation to smoking. *Respir Med*, 108:1633–40.
- Pertl D et al. (2014). Effectiveness and efficacy of minimally invasive lung volume reduction surgery for emphysema. *GMS Health Technol Assess*, 10:Doc01.
- Pietzsch JB, Garner A, Herth FJ (2014). Cost-effectiveness of endobronchial valve therapy for severe emphysema: a model-based projection based on the VENT study. *Respiration*, 88:389–98.
- Pinto A et al. (2010). Home telemonitoring of non-invasive ventilation decreases healthcare utilisation in a prospective controlled trial of patients with amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry*, 81(11):1238–42. doi: 10.1136/jnnp.2010.206680.
- Price LC et al. (2006). UK National COPD Audit 2003: impact of hospital resources and organisation of care on patient outcome following admission for acute COPD exacerbation. *Thorax*, 61:837–42.
- Puhan MA et al. (2011). Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 10:CD005305. doi: 10.1002/14651858.CD005305.pub3.

- Puhan MA et al. (2016). Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 12:CD005305. doi: 10.1002/14651858.CD005305.pub4.
- Ram FS et al. (2004a). Hospital at home for patients with acute exacerbations of chronic obstructive pulmonary disease: systematic review of evidence. *BMJ*, 329:315.
- Ram FS et al. (2004b). Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 1:CD004104.
- Ramsey SD et al. (2007). Updated evaluation of the cost-effectiveness of lung volume reduction surgery. *Chest*, 131:823–32.
- Ribera Salud (2016). *Ribera Salud's contribution to the public healthcare system in Spain*. Valencia, Ribera Salud Grupo.
- Roberts CM et al. (2013). European hospital adherence to GOLD recommendations for chronic obstructive pulmonary disease (COPD) exacerbation admissions. *Thorax*, 68:1169–71.
- Rochester CL, Spanevello A (2014). Heterogeneity of pulmonary rehabilitation: like apples and oranges – both healthy fruit. *Eur Respir J*, 43:1223–6.
- Ruparel M et al. (2016). Understanding variation in length of hospital stay for COPD exacerbation: European COPD audit. *Eur Respir J Open Res*, 2(1):pii:00034–2015.
- Schauer GL et al. (2014). Smoking prevalence and cessation characteristics among U.S. adults with and without COPD: findings from the 2011 Behavioral Risk Factor Surveillance System. *COPD*, 11:697–704.
- Simoens S (2013). Cost-effectiveness of pharmacotherapy for COPD in ambulatory care: a review. *J Eval Clin Pract*, 19:1004–11.
- Simon-Tuval T et al. (2011). Determinants of elevated healthcare utilization in patients with COPD. *Respir Res*, 12:7.
- Smith M et al. (2013). The effect of an active implementation of a disease management programme for chronic obstructive pulmonary disease on healthcare utilization – a cluster-randomised controlled trial. *BMC Health Serv Res*, 13:385.
- Smith KR, Mehta S, Maeusezehl-Fauz M (2004). Indoor air pollution from household solid mass fuel use. In: M Ezzati et al. (eds.) *Comparative quantification of health risks: global and regional health burden of disease attributable to selected major risk factors*. Geneva, World Health Organization.
- Soriano JB et al. (2010). Recent trends in COPD prevalence in Spain: a repeated cross-sectional survey 1997–2007. *Eur Respir J*, 36:758–65.

- Spencer S et al. (2011). Inhaled corticosteroids versus long-acting beta(2)-agonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 10:CD007033.
- Spruit MA et al. (2013). An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med*, 188:e13–64.
- Spruit MA et al. (2014). Differences in content and organisational aspects of pulmonary rehabilitation programmes. *Eur Respir J*, 43:1326–37.
- Stead LF et al. (2013). Physician advice for smoking cessation. *Cochrane Database Syst Rev*, 2:CD000165.
- Steuken LM et al. (2009). Identifying potentially cost effective chronic care programs for people with COPD. *Int J Chron Obstruct Pulmon Dis*, 4:87–100.
- Stoller JK et al. (2010). Oxygen therapy for patients with COPD: current evidence and the long-term oxygen treatment trial. *Chest*, 138:179–87.
- Stone RA et al. (2015). *COPD: Who cares matters*. London, Royal College of Physicians.
- Struik FM et al. (2014). Nocturnal noninvasive positive pressure ventilation in stable COPD: a systematic review and individual patient data meta-analysis. *Respir Med*, 108:329–37.
- Suh ES, Mandal S, Hart N (2013). Admission prevention in COPD: non-pharmacological management. *BMC Med*, 11:247.
- Tashkin DP (2015). Smoking Cessation in Chronic Obstructive Pulmonary Disease. *Semin Respir Crit Care Med*, 36:491–507.
- Turner C (2015). Mobile working: positively engaging community nurses. *Br J Community Nurs*, 20: 134–8.
- Vestbo J, Lange P (2015). Prevention of COPD exacerbations: medications and other controversies. *ERJ Open Res*, 1.
- Vestbo J et al. (2013). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*, 187:347–65.
- Vos T et al. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380:2163–96.
- Walters JA et al. (2010). Action plans with limited patient education only for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 5:CD005074.
- Wong CX, Carson KV, Smith BJ (2012). Home care by outreach nursing for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 3:CD000994.

- Wouters EF (2003). Economic analysis of the Confronting COPD survey: an overview of results. *Respir Med*, 97 suppl C, S3–14.
- Zielinski J et al. (1997). Causes of death in patients with COPD and chronic respiratory failure. *Monaldi Arch Chest Dis*, 52:43–7.
- Zwerink, M et al. (2014). Self management for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 3:CD002990.