Understanding Complexity of Chronic Non-Communicable Diseases: An Integrated Approach for Personalized Management of Patients with COPD

Ingrid M L Augustin1*, Martijn A Spruit1, Frits M E Franssen1 and Emiel F M Wouters1,2

1CIRO+, center of expertise for chronic organ failure, Horn, The Netherlands
2Department of Respiratory Medicine, Maastricht University Medical Center, Maastricht, the Netherlands

Abstract

Non-communicable diseases (NCDs) will increase over the next decades. Understanding the complexity of chronic NCDs and the adaptation of the healthcare system to implement new management strategies addressing the patients’ needs, are still major challenges. Despite all the efforts aligning healthcare delivery with their needs, patients with chronic NCDs are still confronted with fragmented, complex healthcare systems. Healthcare management of NCDs needs a better understanding of the complexity of the disease in order to offer and organize more effective therapies to reduce the huge societal and economic burden of these diseases. In this paper, a patient-centered, personalized healthcare organizational structure for COPD patients with a high disease burden is presented. This could serve as a model for the management of chronic and complex NCDs in general.

KEY ISSUES

- Current guidelines focus on traditional characteristics of the disease condition and ignore the need for an approach regarding the individual as a complex adaptive system.
- Besides the complexity of the illness, the complexity of healthcare is largely neglected in daily practice. Patients and their families continue to navigate in a fragmented, complex healthcare system.
- Dividing patients into groups based on the level of healthcare need has never been done in patient with COPD. GOLD’s COPD classification could be a first step towards that.
- Pulmonary rehabilitation meets the complex needs of patients with COPD and really offers personalized medicine in clinical practice. Although the definition of pulmonary rehabilitation is widely accepted, huge variability still exists in content and organizational aspects.

• A flexible, holistic, and integrated intervention requires a process-based organization: the sociotechnical theory offers a framework for healthcare organizations to create value by improving outcomes. As such, its designed to address the increasing complexity of organizations.

• Concepts of complex adaptive systems are described for COPD as a model for chronic illness conditions. Pulmonary rehabilitation can offer a holistic approach by considering patients as complex adaptive systems.

INTRODUCTION

Cardiovascular diseases, cancers, chronic respiratory diseases and diabetes are the four major chronic non-communicable diseases (NCDs). Together, they represent a major global health burden. Indeed, these NCDs are responsible for 36 million annual deaths or 63% of the total number of deaths [1]. The total number of annual NCD-related deaths is projected to increase up to 53 million by 2030 due to the growth of population and the increased longevity [1]. To a large extent, NCDs develop as a result of an unhealthy lifestyle, such as tobacco use, physical inactivity, unhealthy diet and/or the excessive use of alcohol [1]. These lifestyle conditions, at least in part, seem related to a lower socioeconomic status [1]. The risk factors for the major NCDs are still increasing worldwide and even a general pattern of health style improvement will only result in positive effects decades from now [2]. Therefore, the World Health Organization (WHO) global strategy not only focuses on surveillance and prevention, but considers healthcare management as the third key component of an integrated approach to tackle NCDs [3].

One of the biggest challenges in healthcare management is to understand the growing complexity of these chronic NCDs. Besides understanding the complexity of gene-environment interactions, NCDs manifest in different phenotypic appearances during the disease history as a consequence of irreversibility of pathophysiological changes and the absence of disease-modifying interventions [4]. Current healthcare ignores this heterogeneity in the burden of NCDs and largely fails to offer a personalized, patient-centered approach. Furthermore, personalized interventions are generally evaluated on direct medical costs, thereby following the usual approach in acute medical interventions, but ignoring the lifespan impact of patient-centered and demand-driven disease management. In this opinion paper, future management strategies for patients with Chronic Obstructive Pulmonary Disease (COPD) are discussed as a possible model of management of complex chronic NCDs in general.

The Burden of COPD

COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases [5]. Intriguingly, the Burden of Obstructive Lung Disease program (BOLD) shows a substantial prevalence of COPD among never-smokers (3-11%) [6]. This may be due to occupational and environmental exposures, lifestyle and/or genetic factors [7].

In European cities, 5-10% of adults aged over 40 years has COPD with a higher prevalence in men than in women [7]. In people aged >70 years, the prevalence of COPD is about 20% in men and 15% in women [7]. Overall, COPD mortality rate for men and women in Europe is about 18 per 100 000 inhabitants per year [7]. COPD is associated with a significant economic burden. In the European Union, the total direct costs for respiratory diseases are estimated to be about 6% of the total healthcare budget, with COPD accounting for 56% (38.6 billion Euros) of these costs [7].

In the United States, COPD is, the third leading cause of death behind cancer and heart disease, with an age-adjusted death rate of 41.2 per 100,000 population in 2009 [8]. The American Lung Association shows an aged-adjusted prevalence for adults of 5.2% for men and 7.2% for women [8]. Data taken from the Burden of Obstructive Lung Disease (BOLD) project demonstrate for the United States a prevalence of about 12.7% for men and 15.6% for women aged over 40 years [6, 9]. In people aged >70 years 19.2% of men and 29.6% of women have COPD [6]. In the United States, the annual costs for COPD in 2010 were $49.9 billion. This includes $29.5 billion in direct health care expenditures, $8.0 billion in indirect morbidity costs and $12.4 billion in indirect mortality costs [8].

In 1990, COPD was the twelfth leading cause of Disability-Adjusted Life Years (DALYs) lost in the world, responsible for 2.1% of the total. According to the projections, COPD will be the seventh leading cause of DALYs lost worldwide in 2030 [10]. Indeed, COPD will become the fifth largest disease burden and the fourth greatest cause of death by 2030 [11].

Improving the Management of COPD: Towards Disease Phenotyping

It is widely recognized that COPD is a complex syndrome with numerous pulmonary and extra-pulmonary components [12]. COPD, diagnosed by assessment of the degree of airflow limitation, is nowadays considered as identification of the COPD syndrome without offering any information about disease burden or complexity [12]. Significant heterogeneity exists with respect to clinical presentation, physiology, imaging, response to therapy, decline in lung function, and survival amongst patients with COPD, irrespective of the degree of airflow limitation [12]. Exacerbations and comorbidities contribute to the overall disease severity in individual patients [5].

The global Strategy for the Diagnosis, Management and Prevention of COPD (GOLD) has proposed a three-domain assessment of COPD (Figure 1), which, besides the severity of airflow limitation, also includes the level of symptoms experienced by the patient and the previous history of exacerbations and hospital admissions [5].

Patients are stratified in 4 groups (A, B, C or D) based on these parameters. This approach reflects a pragmatic, expert-based patient stratification, which requires prospective validation in a wide variety of patients with COPD [5]. The GOLD assessment scheme largely aims to support formulation of pharmacological therapies in the different groups of patients with COPD, but offers no tools to assess the individual disease burden in order
to set-up appropriate management strategies, including non-pharmacological interventions and diagnosis/treatment of comorbidities. Indeed, exercise capacity, lower-limb muscle function, health status, problematic activities of daily life, and objectified comorbidities varied to a great extent in a sample of patients with COPD consisting only of GOLD group D [13].

To date, it is widely recognized that identification and subsequent grouping of key attributes of COPD into clinically meaningful and useful subgroups or phenotypes is needed in order to guide more effective therapies and management strategies. A COPD phenotype should be able to classify patients into distinct subgroups that provide prognostic information and allow more appropriate therapy that alters clinically meaningful outcomes [12]. This concept of clinical COPD phenotypes is based on the description of differences between individuals with COPD by a single or a combination of disease attributes [12]. Ideally, assessment of the complexity of COPD needs to include, not only the degree of impairment in the diseased organ, but also the extra-pulmonary components, comorbidities, and environmental factors and their impact on the individual patient. For example, five clusters of comorbidities were identified in patients with COPD entering pulmonary rehabilitation: a cluster with less comorbidity, a cardiovascular cluster, a cachectic cluster, a metabolic cluster, and a psychological cluster [14]. These data emphasize that comorbidities co-occur in patients with COPD. Moreover, the psychological cluster stresses the importance to include the psychological and emotional impact of COPD. The assessment and management of patients with COPD will have to consider this disease heterogeneity in order to provide the best possible care to individual patients. Phenotyping of COPD patients linked with clinically relevant outcome parameters and medical consumption criteria offers perspectives for better and more efficient healthcare management.

Toward Individualized COPD Management

Despite its limitations [15], applying GOLD’s three-domain assessment system illustrates in part the heterogeneity in disease burden in different samples of patients with COPD. Depending on the sample studied, the prevalence of the different GOLD categories varies. In a sample from the general population, group A is the most prevalent (77%). [16]. On the one hand, in patients with COPD treated in primary, secondary and/or tertiary care settings, the proportion of GOLD group A seems clearly lower (about one-third) [17-21]. On the other hand, about one-third of the patients with COPD in primary/secondary/tertiary care settings are identified by severe airflow limitation, high symptom scores and high-risk profile [17-21]. Although to date limited data are available on the stability of the GOLD classification over time, these GOLD categories seem relatively stable over time [18]. These studies not only reflect the heterogeneity of COPD itself, but also the enormous spread in disease burden irrespective of the levels in care organization. As the current GOLD classification largely focuses on pharmacological therapy of COPD, the possibilities of this classification for organization of a demand-driven integrated healthcare management still remain unexplored. Future studies are needed to explore this option and to validate the currently applied markers as reflective for the experienced individual burden of COPD.

**The Current Healthcare Organization for Chronic Conditions**

Current GOLD disease management strategies clearly reflect the persistent emphasis on diagnosis, thereby ruling out other serious diseases and symptom-relieving treatments. They rely on patient-initiated visits, relief of symptoms, normalization of lung function, assurance that there is no urgent medical crisis, and on prevention and treatment of acute or chronic emergencies as exacerbations. In this medically oriented approach, clinical judgment is directed to achieve diagnostic and therapeutic certainty, based on reductionist thinking to break down the clinical problem in circumscribed domains or parameters [22,23]. Such an approach only partly fits with patient-centered
goals of chronic care: enhancement of functional status, minimization of distressing symptoms, enhancement of quality of life, and prolongation of life [24]. Nevertheless, many factors influencing the quality of healthcare are largely overlooked: psychosocial distress often remains undetected or inadequately managed; whereas insufficient attention for education, relevant skills, motivation, and feedback will lead to failures in self-management of the disease or risk factors as a result of patient non-engagement and/or ignorance [25]. Particularly in the management of patients suffering from chronic diseases, it is very important to view a human being as composed of and operating within multiple interacting and self-adjusting systems, including biochemical, cellular, physiological, psychological and social systems. Illness arises from the dynamic interaction within and between these systems, and not from a failure of a single component as chronic airflow limitation in COPD [22].

Current guidelines focus on traditional characteristics of the disease condition itself. They ignore the need to apply a more holistic approach for the individual patient and the need to create an approach of the individual as a complex adaptive system (CAS), thus implying diversity consisting of a wide variety of elements (complex) and implying the capacity to change the ability to learn from experience (adaptive) [26]. To overcome diagnostic and therapeutic uncertainty, the premise of most guidelines is to focus on evidence-based medicine, defined as the conscientious, explicit and judicious use of current best evidence in making decisions about individual patient care [27,28]. More specifically, evidence-based medicine is defined as the use of mathematical estimates of the risk of benefit and harm, derived from high-quality research on population samples, to inform clinical decision-making in the diagnosis, investigation or management of individual patients [29]. Evidence-based medicine relies therefore on predictable, quantitative research, especially from randomized clinical trials (RCTs). Many studies have criticized the extrapolation of these outcomes to real-life conditions, based on the huge selection of patients to become part of these trials. Particularly since primary care COPD patients stand out from patients enrolled in large RCTs in terms of gender, lung function, quality of life and exacerbations [30,31].

However, clinical judgment involves an irreducible element of factual uncertainty and relies to a greater or lesser extent on the interpretation of the illness’ wider history [29]. Maintenance or re-establishment of health can be achieved through a holistic approach of the illness [22]. Effective clinical decision-making in such a complex system must accept unpredictability and is built on subtle emergent forces within the overall system: a small change in one part of the network of interacting systems may lead to a much larger change in another part through amplification effects [22].

The effectiveness of such interventions is highly dependent on the context in which healthcare is delivered [23]. Besides the complexity of the illness, the complexity of healthcare is largely neglected in daily practice. Many factors interact in healthcare, including patient factors (e.g., personal, cultural, socioeconomic), factors related to the healthcare professionals (e.g., training, expertise, interests), task-related factors (e.g., the particular healthcare task, workflow, available time and technology), team-related factors (e.g., communication, roles, leadership), environmental factors (e.g., physical, social and pollution), and organizational factors (e.g., organizational structure, culture, policies and procedures) [32].

Although the interest in organizational contributions to the delivery of care has risen significantly in recent years, coordination of medical resources for patients across the entire delivery system is still a tremendous challenge [33]. Despite recognition of the importance of healthcare organizations and growing research on the relationship between organizational aspects and quality of healthcare, no clear conclusions have emerged from the literature [34]. In current health services research, theory plays a minor role and methodological approaches are mainly focused on cross-sectional, quantitative designs. Another methodological short coming of research is the restricted attention to a single organizational level, thereby failing to take into consideration the nested structure of healthcare organizations and the consequences of such nesting for quality of care [34]. Theories, methodologies and data are needed to link all the three components of structure, process and outcome together, instead of looking for structure-outcome, structure-process and/or process-outcome relationships [34].

In 2001, the Institute of Medicine (IOM) already identified that patients and their families must try to navigate in a fragmented, complex healthcare system with insufficient information and an unclear understanding of how to find the best-quality care for their specific needs and wishes. Similarly, healthcare professionals face pressures to improve quality and measurable outcomes without having systems in place that can help them to identify best practices or means of arranging follow-up for a patient’s need across the entire continuum of care. Purchasers largely lack adequate outcomes and/or process characteristics for benchmarking healthcare delivery systems [35].

In conclusion, current management of chronic conditions such as COPD is still largely based on a reductionist thinking and Newton’s ‘clockwork universe’ metaphor for solving clinical and organizational problems [23]. To cope more adequately with the escalating burden of chronic disease conditions, healthcare must respond flexibly to emerging patterns and opportunities [23].

**Heterogeneity of COPD and Organization of Care**

At least in certain subgroups, COPD is a complex medical problem, with dynamic, non-linear interactions between different disease components along time. Heterogeneity indicates that different disease components are present in these patients at different time points of their medical history. This disease heterogeneity is now largely ignored, describing all the efforts pursued in many ways and in differenthealth systems to realize integration and/or coordination of care [36]. The outcome is an academic quandary of definitions and concept analyses surrounding the notion of integration [37]. The wide GOLD stage distribution in patients with COPD managed in primary and secondary care reflects the ignorance of individual burden of needs by the patient in allocation of health care services. Many COPD disease management programs estimating and organizing patients with COPD in echelons and services are still based on a traditional, pathophysiological disease perspective, focused mainly on the degree of airflow limitation [38-40].
Already in 1999, Leutz proposed an integration framework for chronic conditions, enabling a comprehensive approach, which responds to the varied needs of persons with chronic and/or disabling conditions. In this approach, dimensions of need are defined in terms of stability and severity of the patient’s conditions, duration of illness, urgency of the intervention, scope of services required, and the user’s capacity for self-direction [41]. Following this line of reasoning, Leutz divided service users into three groups: those with mild-to-moderate but stable conditions, those with moderate levels of need, and those with long-term, severe, unstable conditions who frequently require urgent interventions and who have limited capacity for self-direction [41]. Particularly, the latter group will benefit from a high level of integration of the different service domains operating as multidisciplinary teams [41]. Bodenheimer and colleagues applied these concepts in a population management model and divided patients with chronic conditions into three distinct groups based on their degree of need [42]. Patients at level 1 have a relatively low level of health care needs: their chronic condition is reasonably under control, with support for self-management of their chronic condition provided through a primary care team. Level 2 patients are considered at increased risk because their condition is unstable or because they can deteriorate, unless they have structured support through specialist management. Finally, level 3 persons include individuals with highly complex needs and/or high intensity of unplanned secondary care: these persons require active management through case managers [42]. Therefore, the application of a stratified, population-based care model can create a much more efficient, patient-directed care management approach and can offer an appropriate response to the exponentially increasing economical and societal burden of chronic diseases as COPD [2, 7, 10, 43]. Stratifications of diseased populations as proposed by Leutz [41] and Bodenheimer and colleagues [42] have never been done in patients with COPD. GOLD’s COPD classification system is a first step towards that direction, but clearly needs further sophistication, validation, and implementation in order to improve quality of COPD care. Not with standing, it remains a great step forward compared to earlier GOLD classifications, which were solely based on the degree of airflow limitation.

Pulmonary Rehabilitation: Targeting Complex Needs

A patient-centered approach of patients with chronic respiratory diseases such as COPD is not new in pulmonary medicine. Indeed, the first authoritative statement of pulmonary rehabilitation from the American College of Chest Physicians, published in 1974, introduced pulmonary rehabilitation already as an art of medical practice, wherein an individually tailored, multidisciplinary program was formulated. Through accurate diagnosis, therapy, emotional support and education, this program stabilizes or reverses both physiopathological and psychopathological manifestations of pulmonary diseases. Also, it attempts to return the patient to the highest possible functional capacity allowed by the handicap and overall life situation [44]. In 1994, the National Institutes of Health defined pulmonary rehabilitation as a multidimensional continuum of services for the patient and the family supplied by an integrated team of specialists in complementary disciplines, with the goal of the patient living and functioning independently within society [45]. The 2013 ATS/ERS statement defined pulmonary rehabilitation as a comprehensive intervention based on thorough assessment followed by patient-tailored therapies designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors [46]. The latter part of the definition fits with the definition provided in the addendum in the American Association for Respiratory Care stipulating that pulmonary rehabilitation should be both restorative and preventive [47].

The main common points among the various definitions of pulmonary rehabilitation include (1) a focus on chronic respiratory patients and their caregivers; (2) an individualization of the intervention; (3) an ongoing multidisciplinary intervention; (4) outcomes based on physiological, psychological and social measures considering a global dimension to the individual’s health; and (5) the stimulation of long-term adherence to health-enhancing behaviors in order to promote autonomy and social participation of the patient. The diagnosis of physiopathological and psychopathological problems in the individual patient forms the start of every pulmonary rehabilitation program as illustrated in figure 2.

More recently, control panels for personalized medicine of chronic diseases as COPD were suggested: in fact, these so-called control panels are not new and already applied for more than half of a century in dedicated pulmonary rehabilitation settings [48]. Pulmonary rehabilitation is therefore more than a path to personalized medicine in COPD. It really offers...

Figure 2 Shows the different domains of an integrated assessment: determining the complexity of the disease is not the result of one measurement within one domain, but the combination of the measurements at risk (yellow) or impaired (red) of all domains. It means that one measurement in one of the domains showing no problem (green) is not illustrative for the degree of complexity of the disease.
personalized medicine in clinical practice! [49]. Assessment of available pulmonary rehabilitation services stresses the need for evaluation of the psychopathological impact of the disease condition [46].

Although definitions of pulmonary rehabilitation are widely accepted, huge variability exists in content and organizational aspects among pulmonary rehabilitation programs, largely the result of local conditions and financial resources [50]. A recent international survey clearly illustrates the large differences among pulmonary rehabilitation programs across continents including the composition of the rehabilitation teams [50]. The survey also illustrates that most programs are small-scale interventions (median 40 to 75 enrolled individuals per program per year) and that most teams consisted of a median of 5 health care professionals: chest physicians, dieticians, nurses and physiotherapists were the most prevalent team members [50]. The individualization of the goals of pulmonary rehabilitation is not reflected in the selection of the three most important outcomes as identified by healthcare professionals: health status, dyspnea, and exercise capacity [50]. Even mono-disciplinary and strictly educational programs are still described as pulmonary rehabilitation programs, completely neglecting the individualized assessment and multidisciplinary intervention [40,51,52]. Furthermore, the absence of real performance and process metrics hampers meaningful comparisons and benchmarking among programs in different jurisdictions, and does not allow quality control to ensure appropriate standards for pulmonary rehabilitation.

The Process of Pulmonary Rehabilitation: COPD Management Beyond the Control Panel

Pulmonary rehabilitation advocates a personalized approach and aims for patients with COPD to acquire and apply participatory and preventive skills to make them, together with healthcare professionals, more pro-active in the daily management of their disease. This process of healthcare organization around the patient, i.e. to adopt a patient-centered approach, is generally underestimated or neglected in the management of patients with chronic conditions as COPD [53].

Ideally, COPD management must offer a flexible, holistic, and integrated intervention, based on partnering of different skills to achieve shared, individualized, patient-related objectives, and to achieve improvement in clinically relevant outcomes and added value to the patient and the community. This requires a process-based organization to manage business around these core processes (e.g. intake and assessment, rehabilitative therapies, and outcome evaluation) [54].

The sociotechnical systems theory has been developed to design and change organizations in relation to the environmental conditions and strategic choices, and to address the increasing complexity of organizations as a result of increasing external uncertainty and variation within the internal division of labor, as required offering a tailor-made, individualized program [55]. The sociotechnical theory offers a framework to improve efficiency, quality, flexibility and innovation [55]. Indeed, a key feature of sociotechnical design involves bringing together people from different roles and disciplinary backgrounds who have different skills, experience and expertise. Pluralism is the norm, and this implies that they share their views and expertise. They need to educate one another in the opportunities that may exist for the design of a new system, and what they have to offer the design process [56]. Actually, the sociotechnical theory offers a framework for healthcare organizations to create value by

![Figure 3](image-url)
improving outcomes that matter most to patients relative to the costs of achieving those outcomes [57]. The holistic approach of the process, like pulmonary rehabilitation, means organizing around the customer and the need: it has the features of an integrated practice unit (IPU) that treats not only a disease but also the related conditions, complications, and circumstances that commonly occur along with it. In an IPU, personnel regularly work together as a team towards the common goal of maximizing the patient’s overall outcomes as efficiently as possible. Actually, organizing pulmonary rehabilitation according to the sociotechnical principles meets the features of a high-value healthcare organization [58].

Figure 3 illustrates an example of a patient-tailored program, composed by different modules. Each module exists of different therapies in order to achieve the goal of the specific module, which consequently contributes to the medical outcome and the patients’ overall goal of treatment. The basic modules can be supplemented by specific burden-assessment-driven modules. This modular approach makes it possible to individualize the treatment. Figure 4 depicts the integrated baseline assessment, by which the degree of the complexity of COPD is determined, and in turn it depicts the treatment program with its specific modules. Depending on the individual needs and wishes of the COPD patient, each program will differ.

Pulmonary rehabilitation can offer a holistic approach by considering patients as complex adaptive systems: a modular program structure does not mean that illness and patient behavior is modeled as a simple cause and effect system [59]. A patient-centered, demand-driven rehabilitation program aims to seek concordance with the patient [60]. Most patients referred for pulmonary rehabilitation experience a large tension to change: in such circumstances, a small influence can have a large effect in behavior and outcomes [22, 61, 62]. Furthermore, the effectiveness of interventions such as pulmonary rehabilitation will be highly dependent on the context in which the program is delivered [22, 23]. Therefore, all healthcare professionals need to partner with the patient and work closely with other providers to improve the outcomes [53].

CONCLUSIONS

Besides the quantitative burden of chronic NCDs worldwide, the complexity of medicine and healthcare has increased tremendously. The traditional “clockwork universe” in which big problems can be broken down into smaller ones, analyzed and

![Figure 4](https://example.com/fig4.png)

**Figure 4** The process of a patient tailored program: after an integrated baseline assessment, by which the degree of the complexity of COPD is determined, a treatment program is composed of at least all the basic modules. Depending on the individual needs and wishes of the COPD patient, specific burden driven modules can be added. Each individualized program is followed by an outcome measurement of the different domains as described.
solved by rational deduction, still strongly influences the practice of medicine. However, human beings are composed of and operating within multiple interacting and self-adjusting systems and illness arises from the dynamic interaction within and between these systems. The science of complex adaptive systems will provide important concepts and tools for responding to the current challenges in healthcare [23]. Concepts of complex adaptive systems are described for COPD as a model for chronic illness conditions. Pulmonary rehabilitation offers a model for such a holistic approach.

REFERENCES


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