Life expectancy has increased at a rapid pace, partly due to significant improvements in the treatment of communicable diseases, leading to an epidemiologic transition toward higher prevalence of non-communicable diseases. The challenge is not just having longer but healthier lives, thus we have to prepare for the management of chronic diseases. Non-communicable or chronic conditions are characterized by their slow, cumulative progression making them clinically apparent at later stages in life. As age advances, individuals are likely to have more than one co-occurring chronic condition, a phenomenon known as multimorbidity. Healthcare’s traditional approach using different clinical practice guidelines (CPG) does not consider multimorbidity in their recommendations, and if we follow CPG recommendations for each co-occurring disease in a typical elderly patient it will results in the typical prescription of 12 different medications with great potential to develop adverse interactions and increased costs.

COPD AND COMORBIDITIES

Chronic obstructive pulmonary disease is one of the most prevalent chronic diseases worldwide. COPD patients suffer from a high proportion of comorbid conditions and up to two-thirds of individuals suffering from COPD die of non-pulmonary causes, an important observation that could in part explain why despite having effective bronchodilator therapies (the main pharmacologic treatment for COPD) such treatments do not impact all cause mortality.

Patients with COPD have, on average, four to six chronic comorbidities, compared with two to three comorbidities in age-matched controls and the prevalence of such comorbidities are 1.5–2 times higher. In a previous report, our group described the presence of 79 different comorbidities in the BODE COPD cohort. While prevalence of these conditions ranged from 0.1 to 52%, only 12 comorbidities conferred an increased risk of death when co-occurring with COPD and where represented in the form of an orbital graph known as the “Comorbidome” (Solar System). However, the true clinical significance of the other 67 comorbidities may not be adequately assessed by standard regression analysis. In addition, prior reports suggest that comorbidities cluster differently among clinical, demographic and anthropometric characteristics therefore exploring the interactions between comorbidities and those variables could provide a unique opportunity to better understand COPD complexity beyond a single disease perspective.

USING NETWORK SCIENCE TO BETTER UNDERSTAND DISEASE INTERACTIONS

The key to better understanding the complex interaction between diseases and COPD, is by employing an integrative approach combining the different dimensions of diseases. In the case of COPD we can describe the prevalence of comorbidities, their impact on mortality and on patient centered outcomes and cluster patterns. The integration of these variables with the biomedical knowledge of comorbidities may discover a common pathobiological mechanism and potential targets for multimorbidity screening and intervention.

We propose that one approach to this multidimensional problem is the use of Network science, a field focused on the understanding of complex systems by mapping the interconnectivity of such data as objects, persons, proteins, mobile phones or diseases. When any form of bond exists between observations, these observations can be analyzed as forming a network. We have been trained to look at observations as independent entities, in this regard, we have lost sight that many datasets are actually rich in connections between individual data points, which are worth exploring. Networks graphics are composed of individual components called nodes and a grid of interconnecting edges representing associa-
rations between nodes. These interconnected nodes can then be readily visualized revealing the structural basis of the system as either hierarchical, random or scale free networks. The structure of the network will help to identify highly connected individual nodes and specific communities of nodes called modules with great potential applicability.

We present the result of the study titled “COPD Comorbidities Network” (Milky Way) and demonstrated that: 1. Comorbidities are not exclusive of patients with COPD however the prevalence and number of simultaneous comorbidities are higher in COPD. 2. Diseases are interlinked beyond simple coincidence, and aggregate forming modules with meaningful syndromic associations (metabolic syndrome, behavioral/ psychiatric module, among others). The visualization of comorbidities into modules or subnetworks provides clues that are hypothesis generating as they suggest the possibility of shared genetics or pathobiological mechanisms within highly correlated comorbidities. When combining disease modules with clinical characteristics we observed that not all comorbidities affect all COPD individuals similarly. Indeed, age or BMI are correlated with particular types of comorbidities, an observation that has implications for clinicians attempting to relate diseases to specific clinical sub-groups 3. The third important finding of this analysis is that the COPD Comorbidity Network has characteristics of a scale-free architecture revealing the presence of an influential group of highly connected comorbidities (hubs) suggesting an influential or intermediary role. In fact, 23 comorbidities out of 79 hold 72% of the Network’s links and interestingly many of those comorbidities have been shown to influence important outcomes as described in previous studies.[14,15,16].

We believe that the level of technology now available, with computing power that can integrate “large data”, the high throughput world of “omics” (genomics, proteomics, metabolomics) should be viewed as a tool, especially as multimorbidity becomes the norm rather than the exception in an ageing population around the world.

We present the result of the study titled “COPD Comorbidities Network” (Milky Way) and demonstrated that: 1. Comorbidities are not exclusive of patients with COPD however the prevalence and number of simultaneous comorbidities are higher in COPD. 2. Diseases are interlinked beyond simple coincidence, and aggregate forming modules with meaningful syndromic associations (metabolic syndrome, behavioral/ psychiatric module, among others). The visualization of comorbidities into modules or subnetworks provides clues that are hypothesis generating as they suggest the possibility of shared genetics or pathobiological mechanisms within highly correlated comorbidities. When combining disease modules with clinical characteristics we observed that not all comorbidities affect all COPD individuals similarly. Indeed, age or BMI are correlated with particular types of comorbidities, an observation that has implications for clinicians attempting to relate diseases to specific clinical sub-groups 3. The third important finding of this analysis is that the COPD Comorbidity Network has characteristics of a scale-free architecture revealing the presence of an influential group of highly connected comorbidities (hubs) suggesting an influential or intermediary role. In fact, 23 comorbidities out of 79 hold 72% of the Network’s links and interestingly many of those comorbidities have been shown to influence important outcomes as described in previous studies.[14,15,16].

We believe that the level of technology now available, with computing power that can integrate “large data”, the high throughput world of “omics” (genomics, proteomics, metabolomics) should be viewed as a tool, especially as multimorbidity becomes the norm rather than the exception in an ageing population around the world.

**References**


