for access to diagnostic spirometry. Because the healthcare sector might not provide long-term supportive care services for severely disabled individuals, COPD may force at least two individuals to leave the workplace – the affected individual and a family member who must now stay home to care for their disabled relative.[62] Since human capital is often the most important national asset for LMICs, the indirect costs of COPD may represent a serious threat to their economy.

Social burden

Since mortality offers only a limited perspective on the human burden of a disease, it is desirable to find other measures of disease burden that are consistent and measurable within and between nations. The GBD study designed a method to estimate the fraction of mortality and disability attributable to major diseases and injuries using a composite measure of the burden of each health problem: the Disability-Adjusted Life Years (DALY).[63] The DALY for a specific condition is the sum of years lost because of premature mortality and years of life lived with disability, adjusted for the severity of disability. The GBD Study found that from 1990 to 2019, COPD was the primary driver of increased DALY worldwide, especially in LMICs.[21,64] The global health burden caused by COPD increasing by 25.7% from 59.2 million DALY in 1990 to 74.4 DALY in 2019 with largest increases in South East Asia, India, Sub-Saharan Africa and South America.[65] In 2005 COPD was the eighth leading cause of DALY lost across the world but by 2013 COPD was ranked as the fifth leading cause of DALY lost.[53,66] In the United States, COPD is the second leading cause of reduced DALY, trailing only ischemic heart disease.[67] Data from GBD 2017 estimated that the DALY rate was 1068.02/100,000 for COPD.[53]

PATHOGENESIS

COPD is the end-result of complex, cumulative and dynamic gene-environment interactions over the lifetime that can damage the lungs and/or alter their normal developmental or aging processes.[7] Understanding the relationships and interactions between the genetic (G) background of the host and varied environmental (E) risk factors over the lifetime (T) requires further investigation. The term GETomics has been recently proposed to illustrate the complex and dynamic series of interactions between Genetics and Environment over Time.[7] According to this GETomics proposal, the end result of a given GxE interaction depends not only on G and E, but also on T, as determined by both the age of the individual at which that particular interaction occurs (development vs aging) and the previous history of GxE interactions that the individual has encountered earlier in her/his life (biological memory).[7]

Environmental risk factors

Cigarette smoking

Cigarette smoking is a key environmental risk factor for COPD. Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV1, and a greater COPD mortality rate than non-smokers.[68] Most COPD studies have included patients with a cigarette exposure of a minimum of 10 pack-years. However, one study has suggested that even at reduced smoking exposure (<10 pack-years) the 5-year risk of developing COPD is increased in middle-aged adults, and these individuals have an increased risk of severe exacerbation and early death.[69] Yet fewer than 50% of heavy smokers develop COPD[70] and it is estimated that half of all COPD cases worldwide are due to risk factors other than tobacco so other pathogenic factors beyond smoking need to be considered.[9]

Genetics modify the risk of COPD in smokers, but there may also be other risk factors involved. For example, gender and social pressure may influence whether a person takes up smoking or experiences certain occupational or environmental exposures; socioeconomic status may be linked to birthweight (which may impact lung growth and development, and in turn susceptibility to developing COPD);[71] and longer life expectancy will allow greater lifetime