Comorbidities and covid-19
Better understanding is essential for health system planning

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Over 530 million people worldwide are estimated to have had covid-19 by June 2022, resulting in more than 6.3 million deaths. Although most people have few symptoms or mild to moderate illness, a substantial minority are at higher risk of more severe disease (requiring hospital admission) and adverse outcomes, including death and long covid. This is particularly true for people with comorbidities. Our understanding of which conditions increase risk, and their relative importance to adverse outcomes is still evolving.

Initial case series, often unadjusted and with limited generalisability, provided preliminary insights. Subsequently, increasing numbers of higher quality observational studies have attempted to unpick these associations. The US Centers for Disease Control and Prevention regularly reviews all such studies to update the list of conditions associated with greater risk of severe covid-19 and death. While risks generally increase with age and are higher among men, strong evidence now shows increased risks for people with various health conditions, including chronic kidney disease, diabetes, lung and liver diseases, cardiovascular disease, obesity, immunodeficiency, certain disabilities, and mental health conditions.

Risks are highest for people with complicated diabetes, obesity, and anxiety related disorders (relative risk about 1.3 compared with people without these conditions), and less for those with cardiovascular disease (relative risk roughly 1.1). Evidence is more limited for other conditions such as overweight, sickle cell disease, and substance use disorders and inconsistent for asthma, hypertension, and viral hepatitis. Although the exact mechanisms by which pre-existing conditions influence disease susceptibility and severity are not known, inflammatory and hormonal pathways are postulated, as well as social factors such as living in crowded or institutionalised settings.

One in five people worldwide are estimated to be at higher risk of adverse covid-19 outcomes based on the prevalence of chronic conditions. The risk also increases with age and with greater number of underlying conditions. Compared with someone younger than 40 years, the risk of death increases fourfold for people aged 50-64, and more than 10-fold for those aged over 85. Similarly, compared with people with no underlying conditions, the risk of death is 1.5 and 3.8 times higher for those with one comorbidity and over 10 comorbidities, respectively. These findings have been used to develop multiple risk score calculators to aid clinical decisions.

Long term effects
Although most people with covid-19 recover fully, some have longer term symptoms (long covid)—usually persisting beyond 35 weeks. Both the definition and estimated prevalence of long covid vary widely, but one recent international systematic review of studies reported that around 43% of adults with covid-19 still have at least one symptom 28 days after infection, rising to 57% among those admitted to hospital. Symptoms of long covid are wide ranging but most commonly include fatigue, anosmia, dyspnoea, cough, and myalgia. A UK analysis of primary care records for 486 149 community patients with confirmed covid-19 showed that reporting persistent symptoms beyond 12 weeks was associated with many pre-existing conditions, including chronic obstructive pulmonary disease, fibromyalgia, anxiety, and coeliac disease, in addition to risk factors such as obesity, tobacco smoking, being female, and socioeconomic deprivation. Furthermore, evidence is growing that new chronic diseases can occur after acute covid-19. Data from a US administrative claims database showed that 14% of adults who had had covid-19 developed new clinical conditions within six months; a 1.65% higher incidence than that seen after other viral infections. Clinical sequelae included interstitial lung disease, respiratory failure, congestive heart failure, arrhythmia, and type 2 diabetes. The cluster of symptoms and clinical outcomes differed by age, between men and women, and between those who were and were not admitted to hospital. Risk of SARS-CoV-2 infection, severe disease, and death have reduced in populations with high vaccine uptake. Nevertheless, breakthrough infection still occurs, and there is some evidence that older people (>65 years) and those with underlying conditions remain at greatest risk, possibly because vaccine effectiveness wanes more quickly in these groups. Vaccines also reduce the risk and duration of long covid symptoms, but the effect is smaller than the reduction in mortality and severe disease.

We now have a better understanding of the conditions that increase risk of severe covid-19, but unanswered questions remain about their role in longer term outcomes. A better quantification of the relation between comorbidities and different outcomes and...
the populations at risk is essential for future health system planning. Such information will also support policy decisions, allowing consideration of the differential economic, social, and health effects of protective interventions, including societal restriction.

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