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EDITORIALS

Covid-19: risk factors for severe disease and death

A long list is emerging from largely unadjusted analyses, with age near the top

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As the covid-19 pandemic accelerates, governments are warning people at high risk to be particularly stringent in observing social distancing measures because if they become ill they are more likely to need critical care including ventilation, and to die.[1] Most data on covid-19 are from China, and although most confirmed cases have been classified as mild or moderate, 14% are severe and 5% critical.[2] Case fatality rates are difficult to assess with certainty but could be as high as 1%,[3 4] which is much greater than seasonal influenza at about 0.1%.

Up to 25% of people in the United Kingdom are designated high risk—including all adults aged over 70 and those with underlying health conditions such as respiratory and cardiovascular disease, and cancer.[5] Strict restrictions are now in place for everyone, reducing movement outside the home to an absolute minimum, except for essential workers.[6] These measures will be in place for weeks, possibly months. Among vulnerable groups including older adults, such severe restrictions are likely to lead to further loneliness, isolation, and loss of mental and physical function.

Evidence is rapidly accumulating about covid-19 and its causal agent SARS-CoV-2. In a linked study, Chen and colleagues (doi:10.1136/bmj.m1091) report on the first 799 people with the disease who were admitted to the isolation ward of a hospital in Wuhan, China, assigned for patients with severe or critical covid-19.[7] The authors compared the characteristics of 113 (14.4%) patients who have died so far with those of 161 patients who recovered, finding that those who died were on average 17 years older (with no deaths among those aged under 40 and 16.8% of deaths among those aged 40-60), more likely to be male, and more likely to have a comorbidity such as hypertension, diabetes, cardiovascular disease, or chronic lung disease.

These results are similar to many other case series from China.[2 8-11] The largest so far is the China Center for Disease Control and Prevention's report of 44 000 people with laboratory confirmed covid-19. Older age, cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer were all associated with an increased risk of death.[2] A meta-analysis of eight studies including 46 248 patients with laboratory confirmed covid-19 indicated that those with the most severe disease were more likely to have hypertension (odds ratio 2.36 (95% confidence interval 1.46 to 3.83)), respiratory disease (2.46 (1.76 to 3.44)), and cardiovascular disease (3.42 (1.88 to 6.22)).[12]

In other studies, obesity and smoking were associated with increased risks.[10 11] In Italy, higher risks have also been reported in men than in women,[13] which could be partly due to their higher smoking rates and subsequent comorbidities.

However, the relative importance of different underlying health conditions is unclear, owing to inadequate adjustment for important confounding factors such as age, sex, and smoking status; insufficient follow-up[14]; and likely under-reporting of pre-existing conditions. In China, health records are often incomplete or inaccurate and chronic conditions are underdiagnosed.[15 16]

Even when smoking status is reported, data appear incomplete. Only 7% of the population in Chen and colleagues' study identified as ever smokers (defined as ≥30 pack years), whereas smoking prevalence among Chinese men is over 60%.[17] Finally, these studies are mainly among those patients at the highest risk, admitted to hospital with full testing. Findings might not apply to the general population.

As yet, there are no good data on how the risks associated with underlying comorbidities might vary in different population groups or settings. Unlike other viruses, symptomatic infections are uncommon in children and, although not resistant,[18] children are at low risk of severe disease. Based on current data, the mean case fatality rate for adults aged under 60 is estimated to be less than 0.2%, compared with 9.3% in those aged over 80.[4] Even if comorbidities increased mortality risk by five times, risk would remain lower for younger people than for most older adults.

As we await more data, government guidance draws on knowledge of risk factors for other similar infections such as influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome. Although younger people appear generally at lower risk, everyone must adhere to government restrictions to protect the millions of people at higher risk due to age or serious comorbidities.

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In order to minimise future social and economic disruption, high quality data at the population level are urgently needed—as soon as a reliable test for past infection becomes available. All further studies of both past and current infections must include complete and accurate data on all potential risk factors; ideally through electronic healthcare records. Most importantly, data must be gathered and pooled across countries, so we can optimise our understanding.

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