

## Who is most likely to be infected with SARS-CoV-2?

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## Who is most likely to be infected with SARS-CoV-2?

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### TEXT

Despite the daily updates on number of cases, hospitalisations and deaths around the world, and the increasing number of hospital-based case-series, we are still missing some of the fundamental information on how COVID-19 spreads in the population, and who is really at risk of both infection and severe consequences. In the Lancet Infectious Diseases this week, de Lusignan and colleagues report on the characteristics of the first 3800 people tested for COVID-19 within the Royal College of General Practitioners (RCGP) sentinel primary care surveillance network [1]. Unlike most previous studies that examine risk factors for poor prognosis, they report characteristics associated with COVID-19 susceptibility.

The RCGP surveillance system, set-up in 1957, monitors consultations for communicable diseases using a network of 500 GP practices across England which are broadly representative of the population[2]. Twice-weekly automatic data downloads provide a real-time warning of impending epidemics. In January 2020, the network expanded to include the testing for COVID-19 among those presenting with symptoms of influenza or respiratory infection.[3] COVID-19 surveillance data, supplemented with data from contact tracing, or routine NHS services were linked with electronic health records. Of 3802 tests, 587 (15.4%) were positive for COVID-19. Risk of infection was less than 5% in those aged <18 years, but approximately five times as high among people aged 40 years or more. After adjustment for other factors, infection risk was also higher among men (about 1.5 times), those of black ethnicity (5 times), the obese (1.5 times) and those living in more deprived or in urban locations. Surprisingly, household size contributed little. Among chronic comorbidities examined, only those with chronic kidney disease had higher risk of infection, whilst the risk in active smokers was around half that observed in never smokers.

Two other new articles in pre-print have examined population-level risks. An article using the UK Biobank data corroborates the results on age, sex, black ethnicity and obesity as risk factors for

severe infection[4] and a study of 17m patients from UK primary care shows increased risks of in-hospital COVID-19 mortality with age, male sex, obesity, deprivation, ethnic minorities. [5] Conversely, co-morbidities and smoking seem to play a stronger role in poor prognosis[5][6].

As there are still few population level studies, this paper represents an important new contribution and the good quality statistical methods allow quantification of independent risks. However, the data are not fully representative of the general population, excluding those with mild or no symptoms and instead reflecting consultation patterns, with over-representation of women and older people but fewer smokers.[7] Lower consulting thresholds (e.g. among women) could dilute test positivity compared with groups who might consult only if they were more severely ill. It is also possible that there are unmeasured confounders, eg social and workplace exposures, interactions and behaviours which may explain increased risks in some groups.

Unlike other reports [8] this study suggests that gender differences in poor outcomes from COVID-19 are at least partly related to differential disease susceptibility. The role of ethnicity in both greater susceptibility and poorer prognosis is also a growing concern and deserving of further study. It seems that most comorbidities (except chronic kidney disease), whilst important for predicting prognosis, do not play a major role in susceptibility to infection. There is also the thorny issue of smoking to be addressed. It is likely that the results could reflect consulting patterns and the higher rates of non-infectious cough. Smoking seems important as a risk factor for poor prognosis[4] but studies are conflicting and the effect merits further investigation. The one major modifiable risk factor is obesity, which presents a double problem of increasing susceptibility to infection, as well as risk of severe consequences.[9]

What is fundamentally clear, however, is that whatever the specific risk factors, the COVID-19 pandemic exacerbates existing socioeconomic inequalities and this needs both exploration and mitigation in the coming months and years.[10] As we prepare to leave lockdown, knowing who is most at risk of infection is vital. This study highlights the more susceptible sub-groups among those with relevant symptoms, although we cannot be sure of why. Population-level studies with testing among random samples of the general population (irrespective of symptoms), as well as accurate antibody tests of past infection are urgently needed.

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